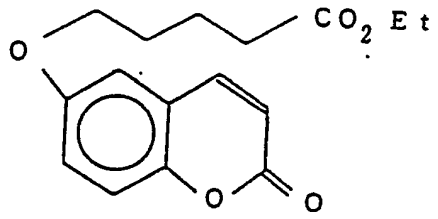
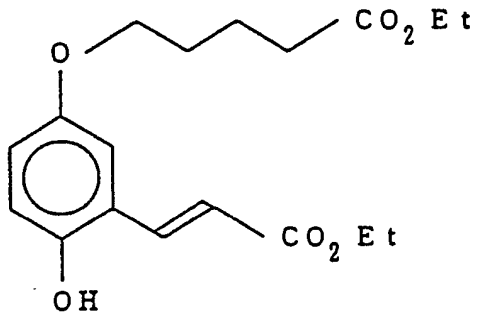


6-Hydroxycoumarin (405 mg; prepared in reference example 25) was dissolved in dry dimethylformamide (6 ml). Sodium hydride (60 mg) was added to the solution. The mixture was reacted for 15 min. Ethyl 5-bromopentanoate (0.48 ml) was added dropwise to the reaction solution. The mixture was stirred for 1 hr at 60 °C. Ice-water was added to the reaction solution. The mixture was acidified with 1N hydrochloric acid. The mixture was extracted with ether. The extract was washed with water, dried anhydrous magnesium sulfate and then evaporated. The residue was purified by column chromatography on silica gel (n-hexane : ethyl acetate = 4 : 1 → 2 : 1) to give the title compound (398 mg) having the following physical data.
NMR: 7.75 (1H, d, J = 10Hz), 7.25 (1H, d, J = 8Hz), 7.10 (1H, dd, J = 8Hz, J = 1HZ), 6.90 (1H, d, J = 1Hz), 6.43 (1H, d, J = 10Hz).

Reference example 27

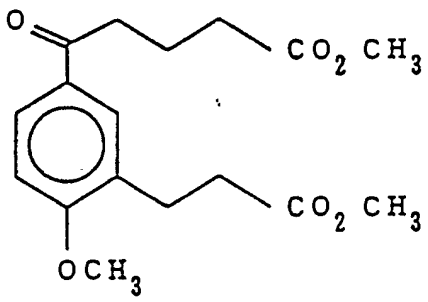
Ethyl 3-[1-hydroxy-4-(4-ethoxycarbonylbutoxy)benzen-2-yl]prop-2E-enoate



Sodium hydride (content : 62%; 60 mg) was gradually added to anhydrous ethanol (10 ml) and dissolved. A solution of the ester (314 mg; prepared in reference example 26) in anhydrous ethanol (1 ml) was added to the solution. The mixture was stirred for 4 hr. at 70 °C and then for 30 min at 80 °C. Glacial acetic acid (210 mg) was added to the reaction solution with ice-cooling to stop the reaction. The solvent was removed from the reaction solution under reduced pressure. The residue was diluted with ether. The mixture was washed with water. Aqueous layer was removed. Ethereal layer was dried over anhydrous magnesium sulfate and then evaporated. The residue was purified by column chromatography on silica gel (n-hexane : ethyl acetate = 2 : 1) to give the title compound (122 mg) hav1Hg the following physical data.
TLC(n-hexane : ethyl acetate = 2 : 1) : Rf 0.20.

Reference example 28

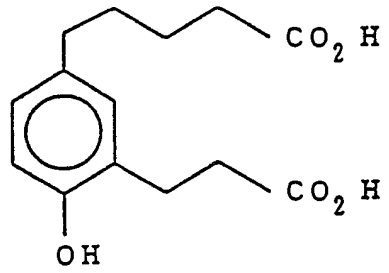
Methyl 3-[1 -methoxy-4-(1-oxo-4-methoxycarbonyl-n-butyl)benzen-2-yl]propionate



Anhydrous aluminium chloride (22.2 g) was suspended in methylene chloride (150 ml). The suspension was cooled to 0 °C. Methyl 4-(chloroformyl)butylate (10.0 g) was added to the suspension at 0 °C. The methyl ester (10.5 g), which was prepared with using 3-(1-methoxybenzen-2-yl)propanoic acid (10.0 g) by the same procedure as reference example 12, was added to the prepared suspension. The suspension was stirred for 30 min. The reaction solution was poured into a mixture of ice and 2N hydrochloric acid. The reaction mixture was extracted with ethyl acetate. The extract was washed with saturated brine, dried over anhydrous magnesium sulfate and then evaporated. The residue was purified by column chromatography on silica gel (n-hexane : ethyl acetate = 2 : 1 → 3 : 2) to give the title compound (13.6 g) having the following physical data.
TLC(n-hexane : ethyl acetate = 2 : 1) : Rf 0.33;
MS : m/z 322 (M^+), 291.

Reference example 29

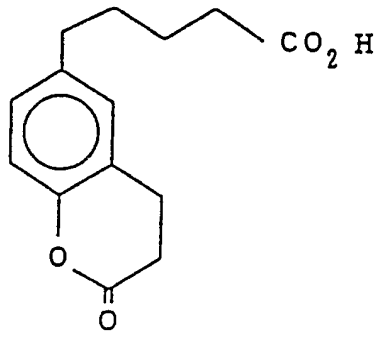
3-[1-hydroxy-4-(4-carboxyl-n-butyl)benzen-2-yl]propionic acid



An ester (1.0 g), which was prepared with using the ester prepared in reference example 28 by the same procedure as reference example 16, was dissolved in dimethylsulfoxide (2 ml). The solution was stirred for 30 min. at 180 °C. The reaction solution was diluted with ether. The mixture was washed with 1 N hydrochloric acid, followed by saturated brine, dried over anhydrous magnesium sulfate and then evaporated. The residue was purified by column chromatography on silica gel (n-hexane : ethyl acetate = 3 : 1) to give an olefin compound. The olefin compound (848 mg) was dissolved in ethanol (15 ml). A suspension of 10% palladium-carbon (100 mg) in ethanol (5 ml) was added to the solution. The mixture was stirred for 1.5 hr. at room temperature in an atmosphere of hydrogen gas. The catalyst was removed from the reaction solution by Celite 545. The reaction solution was evaporated to give a reduced compound (798 mg). Pyridinium chloride (15 g) was added to the reduced compound (1.66 g). The mixture was stirred for 4 hr. at 1 80 °C. A temperature of the reaction mixture was down to room temperature. The mixture was dissolved in 1N hydrochloric acid. The reaction mixture was extracted with ethyl acetate. The extract was washed with saturated brine, dried over anhydrous magnesium sulfate and evaporated to give the residue contained the title compound having the following physical data. The residue was used in next reaction without purification.
TLC(ethyl acetate) : Rf 0.39;
MS : m/z 266 (M^+), 248, 161.

Reference example 30

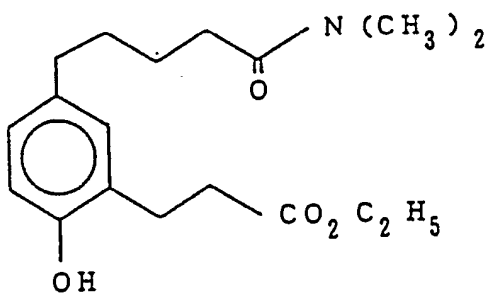
5-(3,4-dihydrocoumarin-6-yl)valeric acid



The dicarboxylic acid (1.72 g) prepared in reference example 29 was dissolved in a mixture of benzene (100 ml) and tetrahydrofuran (2 ml). Dowex 50W x 8 (H^+ form)(about 10 ml) was added to the solution. The mixture was refluxed for 2 hr.. The reaction solution was filtered to remove Dowex. The filtrate was evaporated to give the residue (1.28 g) contained the title compound having the following physical data. The residue was used in next reaction without purification.
TLC(chloroform : methanol = 10 : 1) : Rf 0.49;
MS : m/z 248 (M^+), 230.

Reference example 31

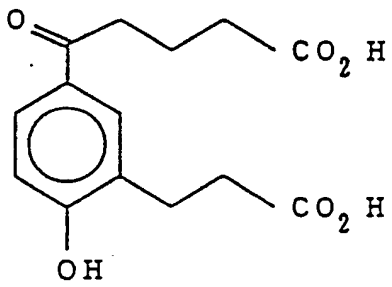
Ethyl 3-[1-hydroxy-4-dimethylaminocarbonyl-n-butyl)benzen-2-yl]propionate



A carboxylic acid, which was prepared with using the lactone prepared in reference example 30 by the same procedure as reference example 6 (with the proviso that dimethylamine was used instead of morpholine) → example 5, was dissolved in ethanol (5 ml). Conc. sulfuric acid (about 0.1 ml) was added dropwise to the solution. The solution was stirred for 1.5 hr. at 60° C. The reaction solution was diluted with ethyl acetate. The diluted solution was washed with saturated aqueous solution of sodium bicarbonate, followed by saturated brine, dried over anhydrous magnesium sulfate and evaporated. The residue was purified by column chromatography on silica gel (ethyl acetate) to give the title compound (1.5 g) having the following physical data.
TLC(ethyl acetate) : Rf 0.58;
MS: m/z 307 (M^+), 276.

Reference example 32

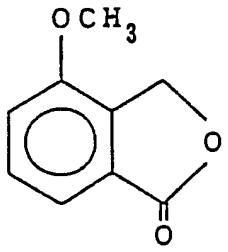
3-[1-hydroxy-4-(1-oxo-4-carboxylbutyl)benzen-2-yl]propionic acid



A dicarboxylic acid (6.6 g), which was prepared with using the ester prepared in reference example 28 by the same procedure as reference example 5, was dissolved in acetic acid (10 ml). 47% hydrobromic acid (30 ml) was added to the solution. The mixture was refluxed all night. The reaction solution was evaporated. The residue was diluted with ethyl acetate. The diluted solution was washed with saturated brine, dried over magnesium sulfate and then evaporate. The residue was recrystallized from ethyl acetate to give the title compound (915 mg) having the following physical data.
MS : m/z 280 (M^+), 262.

Reference example 33

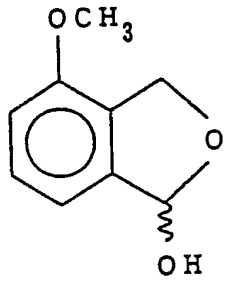
Anhydrous 4-methoxyphthalide



Anhydrous 2-methoxyphthalic acid (640 mg), which was prepared with using anhydrous 2-hydroxyphthalic acid by the same procedure as reference example 12, was suspended in tetrahydrofuran (20 ml). Acetic acid (430 mg) and sodium borohydride (135 mg) were added to the suspension. The mixture was stirred for 30 min. at room temperature and for 2 hr. at 50°C. The reaction solution was cooled. 1N hydrochloric acid (7 ml) was added to the cooled solution. The solution was stirred for 15 min. The reaction solution was evaporated. The residue was purified by column chromatography on silica gel (n-hexane : ethyl acetate = 2 : 1 → 1 : 1) to give the title compound (314 mg) having the following physical data.
TLC(n-hexane : ethyl acetate = 1 : 1) : Rf 0.67.

Reference example 34

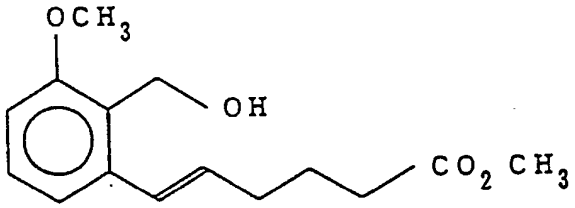
1-hydroxy-4-methoxy-1,3-dihydrobenzo[c]furan



The phthalide (346 mg) prepared in reference example 33 was dissolved in toluene (20 ml). The solution was cooled to -78 °C. A 1.76N solution of diisobutylaluminum hydride (DIBAL) in toluene (1.43 ml) was added dropwise to the cooled solution. The mixture was stirred for 30 min. at -78 °C. Methanol (0.2 ml) was added to the reaction solution to decompose the excess DIBAL. Water was added to the reaction solution. A temperature of the solution was up to room temperature. The solution was stirred for 30 min. at room temperature. The reaction solution was dried over anhydrous sodium sulfate, washed with ethyl acetate and evaporated to give the residue contained the title compound having the following physical data. The residue was used in next reaction without purification.
TLC(n-hexane : ethyl acetate = 1 : 1) : Rf 0.56

Reference example 35

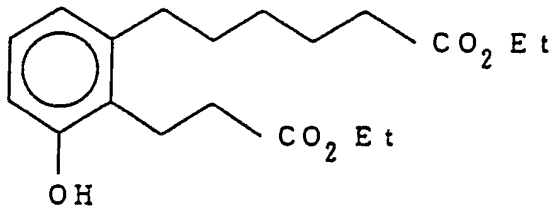
Methyl 5E-6-(2-hydroxymethyl-3-methoxyphenyl)hexenoate



(4-Carboxylbutyl)triphenylphosphonium bromide (2.79 g) was suspended in toluene (30 ml). Potassium t-butoxide (1.34 g) was added to the suspension. The suspension was stirred for 15 min. at 80 °C. A solution of the compound (348 mg) prepared in reference example 34 in toluene (10 ml) was added dropwise to the reaction solution. The solution was stirred for 1.5 hours at 80 °C. The reaction mixture was cooled and then acidified by adding 1 N hydrochloric acid. The solution was extracted with ethyl acetate. The extract was washed with water, dried over anhydrous magnesium sulfate and evaporated. The residue was purified by column chromatography (n-hexane : ethyl acetate = 1 : 1) to give the title compound (270 mg) having the following physical data.
NMR: δ 7.12 (1H, t, J = 8Hz), 7.03 (1H, d, J = 8Hz), 6.85-6.70 (2H, m), 6.05 (1H, d, t, J = 16 Hz, J = 6Hz), 4.80 (2H, s), 3.90 (3H, s);
MS : m/z 250 (M^+), 232.

Reference example 36

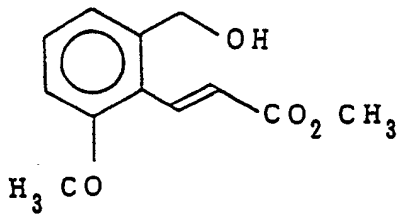
Ethyl 6-[2-(2-ethoxycarbonylethyl)-3-hydroxyphenyl]hexanoate



Methyl 6-[2-(2-ethoxycarbonylethyl)-3-methoxyphenyl]-hexanoate, which was prepared with using the compound prepared in reference example 35 by the same procedure as reference example 12 → reference example 2 → reference example 14 → reference example 1 (with the proviso that ethyl diethylphosphonoacetate was used instead of t-butyl diethylphosphonoacetate) → reference example 2, and pyridine hydrochloride were reacted for 2 hr. at 190 °C. The reaction mixture was cooled. 1N hydrochloric acid was added to the mixture. The mixture was extracted with ethyl acetate. The extract was dried over anhydrous magnesium sulfate and then evaporated. The residue was dissolved in a saturated solution of hydrogen chloride in ethanol (5 ml). The solution was stirred for 30 min. The reaction solution was evaporated. The residue was purified by column chromatography on silica gel (n-hexane : ethyl acetate = 2 : 1) to give the title compound (87.3 mg) having the following physical data.
NMR: δ 7.13 (1H, d, J = 8Hz), 7.03 (1H, t, J = 8Hz), 6.75 (2H, d, J = 8Hz), 4.20-4.05 (4H, m), 2.93 (2H, t, J = 7Hz), 2.70-2.50 (4H, m), 2.30 (2H, t, J = 7Hz), 1 .75-1.30 (6H, m), 1.30-1.20 (6H, m);
MS : m/z 336 (M^+), 291, 262.

Reference example 37

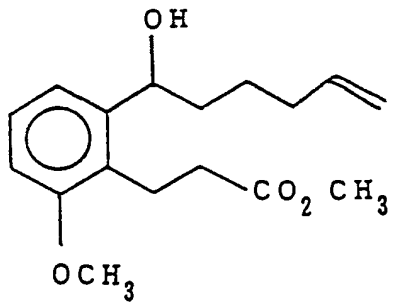
Methyl 2E-3-(2-hydroxymethyl-6-methoxyphenyl)acrylate



1-Hydroxy-7-methoxy-1,3-dihydrobenzo[c]furan (1.08 g), which was prepared with using 7-methoxyphthalide which was synthesized with using 3-methoxybenzaldehyde by the method described in Journal of Organic Chemistry, 1980, 45 , 1835-1838, was dissolved in chloroform (20 ml). Methyl (triphenylphosphoranylidene)acetate (2.68 g) was added to the solution. The mixture was stirred for 40 min. at 50 °C. A temperature of the reaction mixture was down to room temperature. The reaction solution was purified by column chromatography on silica gel (n-hexane : ethyl acetate = 2 : 1) to give the title compound (1.25 g) having the following physical data.
NMR: δ 8.93 (1H, d, J = 16Hz), 7.30 (1H, t, J = 8Hz), 7.07 (1H, d, J = 8Hz), 6.90 (1H, d, J = 8Hz), 6.70 (1H, d, J = 16HZ), 4.80 (2H, d, J = 5Hz), 3.87 (3H, s), 3.81 (3H, s);
MS : m/z 222 (M^+), 204, 191.

Reference example 38

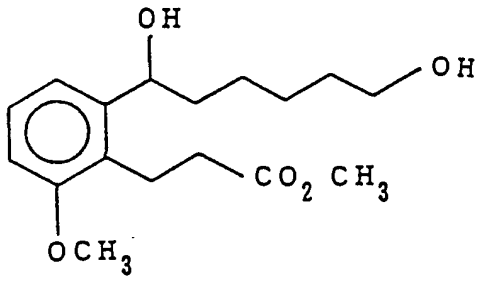
Methyl 3-[2-(1-hydroxyhex-5-enyl)-6-methoxyphenyl]propionate



5-Bromo-1-penten (596 mg) was added dropwise to a solution of magnesium (96 mg) in diethyl ether (2 ml). Diethyl ether (4 ml) was added to the solution to prepare Grignard reagent. A solution of methyl 3-(2-formyl-6-methoxyphenyl)propionate (444 mg), which was prepared with using the ester prepared in reference example 37 by the same procedure as reference example 2 → reference example 14, in diethyl ether (1 ml) was ice-cooled. The grignard reagent (3.3 ml) prepared beforehand was added dropwise to the cooled solution. The mixture was stirred for 1.5 hr. with ice-cooling. The reaction mixture was added to a saturated aqueous solution of ammonium chloride. The mixture was extracted with diethyl ether. The extract was washed with water, dried over anhydrous magnesium sulfate and evaporated. The residue was purified by column chromatography on silica gel (n-hexane : ethyl acetate = 4 : 1) to give the title compound (497.5 mg) having the following physical data.
NMR: δ 7.23 (1H, t, J = 8Hz), 7.10 (1H, d, J = 8Hz), 6.78 (1H, d J = 8Hz), 6.90-6.70 (1H, m), 5.06-4.90 (3H, m), 3.85 (3H, s), 3.67 (3H, s), 3.05-2.95 (2H, m), 2.65-2.52 (2H, m), 2.15-2.05 (2H, m), 1.90-1.35 (4H, m);
MS : m/z 292 (M^+), 260, 243.

Reference example 39

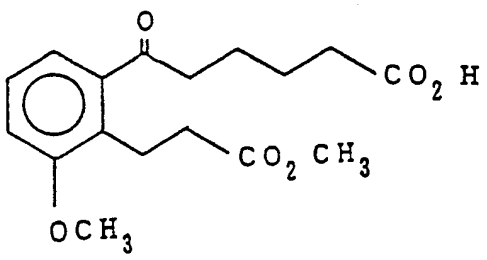
Methyl 3-[2-(1,6-dihydroxyhexyl)-6-methoxyphenyl]propionate



A solution of the ester (494.5 mg) prepared in reference example 38 in tetrahydrofuran (6.77 ml) was ice-cooled. A 1N solution (6.77 ml) of diborane in tetrahydrofuran was added dropwise to the solution. The mixture was stirred for 30 min at room temperature. The reaction solution was ice-cooled. Water was added dropwise to the solution to decompose excess diborane. A 1N aqueous solution of sodium hydroxide and then 30% hydrogen peroxide (6.77 ml) were added dropwised to the reaction mixture. The mixture was stirred for 30 min. at room temperature and reacted by the same procedure as reference example 12. The reaction solution was poured into a 1N solution of hydrochloric acid in diethyl ether (100 ml). The mixture was extracted with diethyl ether. The extract was washed with water, dried over anhydrous magnesium sulfate and then evaporated. The residue was purified by column chromatography on silica gel (n-hexane : ethyl acetate = 2 : 1 → 1 : 1) to give the title compound having the following physical data.
NMR: δ 7.23 (1H, t, J = 8Hz), 7.08 (1H, d, J = 8Hz), 6.78 (1H, d, J = 8Hz), 5.05-4.95 (1H, m), 3.83 (3H, s), 3.67 (3H, s), 3.63 (2H, t, J = 7Hz), 3.05-2.95 (2H, m), 2.65-2.53 (2H, m), 1.90-1.30 (8H, m);
MS : m/z 310 (M^+), 223.

Reference example 40

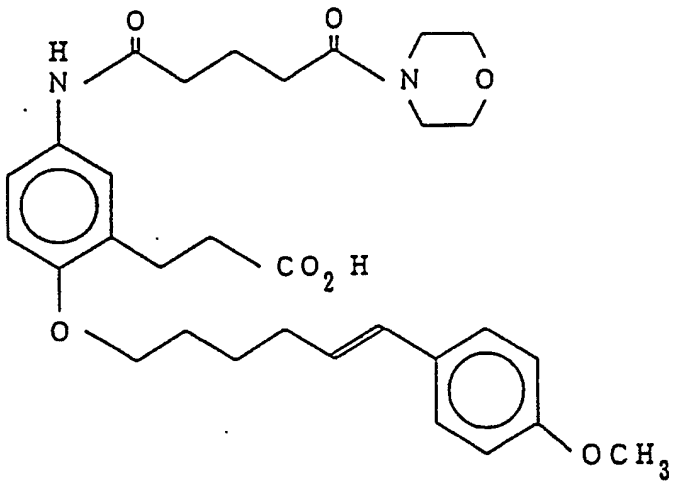
6-Oxo-6-[2-(2-methoxycarbonylethyl)-3-methoxyphenyl]hexanoic acid



A solution of 6-oxo-6-[2-(2-methoxycarbonylethyl)-3-methoxyphenyl]hexanal (450 mg), which was prepared with using the ester prepared in reference example 39 by the same procedure as reference example 14, in acetone (6 ml) was ice-cooled. 2.67N Jone's reagent (2 ml) was added dropwise to the solution. The mixture was stirred for 1 hr. with ice-cooling. Isopropyl alcohol was added to the solution to stop the reaction. Water was added to the solution to dissolve chromic anhydride. The reaction mixture was extracted with diethyl ether. The extract was washed with water, dried over anhydrous magnesium sulfate and then evaporated. The residue was purified by column chromatography on silica gel (n-hexane : ethyl acetate = 2 : 1 → 1 : 1) to give the title compound (369 mg) having the following physical data.
NMR: δ 7.25 (1H, t, J = 8Hz), 7.08 (1H, d. J = 8Hz), 6.95 (1H, d, J = 8Hz), 3.85 (3H, s), 3.67 (3H, s), 3.05-2.95 (4H, m), 2.67-2.55 (2H, m), 2.40 (2H, t, J = 7Hz), 1.85-1.60 (4H, m)

Example 1

3-[1-[6-(4-methoxyphenyl)hex-5E-enyl]oxy-4-(5-oxo-5-morpholinopentanamido)benzen-2-yl]propionic acid



The butyl ester (70 mg; prepared in reference example 6) was dissolved in formic acid (5 ml). The solution was stirred for 5 hr. at room temperature. The reaction solution was evaporated to remove formic acid. The residue was purified by column chromatography on silica gel (ethyl acetate : methanol = 10 : 1) to give the title compound (40 mg) of the present invention, having the following physical data.
TLC(ethyl acetate : methanol = 10 : 1) : Rf 0.10;

IR(cm^{-1}) : ν 3307, 2932, 1723, 1609, 1510, 1245, 1116, 1032.

Example 1(a) - 1(v)

The compounds, of the present invention, shown in the following table 4 were obtained, with using the compounds which were prepared with using the butyl ester prepared in reference example 5 and the corresponding amines by the same procedure as reference example 6 (with the proviso that the corresponding amines were used instead of morpholine) or the compounds which were prepared with using the corresponding appropriate compounds shown in the formula MsO-Z^1-B^2 or Br-Z^2-B^2 (wherein all of the symbols are the same meaning as described hereinbefore) by the same procedure as reference example 4, 5 and 6 (with the proviso that the corresponding amines were used instead of morpholine), by the same procedure as example 1.

Table 4

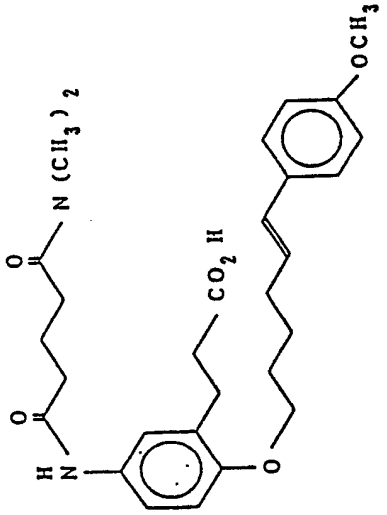
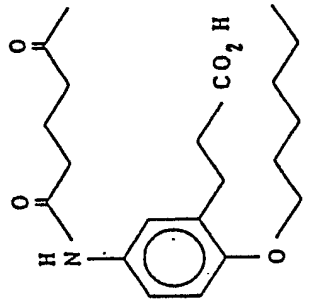
Ex.No.	Structural formula	T L C	I R (cm^{-1})
1 (a)		Rf 0.31 (ethyl acetate: methanol =6:1)	ν 3357. 2952. 1715. 1683. 1662. 1542. 1508. 1471. 1410. 1235. 1176. 1117. 1031. 972. 886. 825
1 (b)		Rf 0.37 (ethyl acetate: methanol =5:1)	ν 3353. 2940. 1704. 1687. 1668. 1554. 1505. 1474. 1422. 1277. 1222. 1200. 1124. 1029. 805

Table 4 (continued)

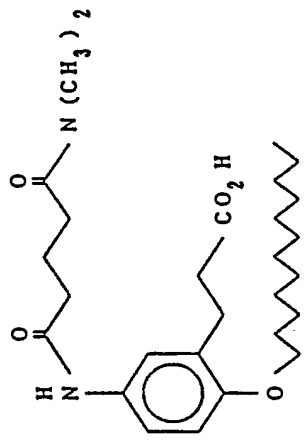
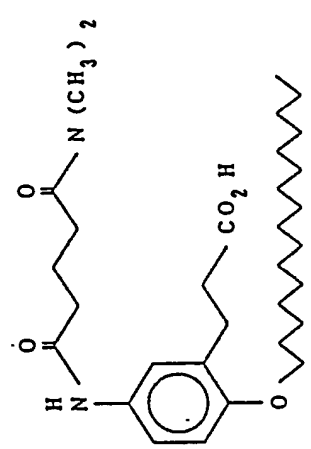
Ex.No.	Structural formula	T L C	I R (cm^{-1})
1 (c)		R f 0.52 (ethyl acetate: methanol = 5:1)	ν 3335. 2923. 2849. 1687. 1607. 1553. 1505. 1473. 1432. 1221. 811
1 (d)		R f 0.53 (ethyl acetate: methanol = 5:1)	ν 3210. 2918. 2850. 1712. 1650. 1605. 1539. 1504. 1473. 1415. 1230. 1116. 1031. 805. 718

Table 4 (continued)

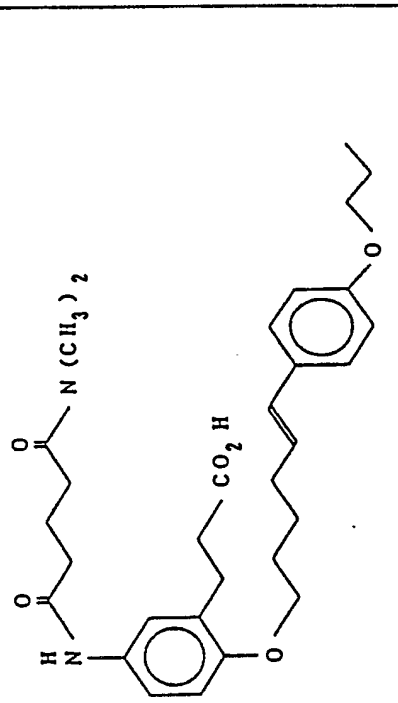
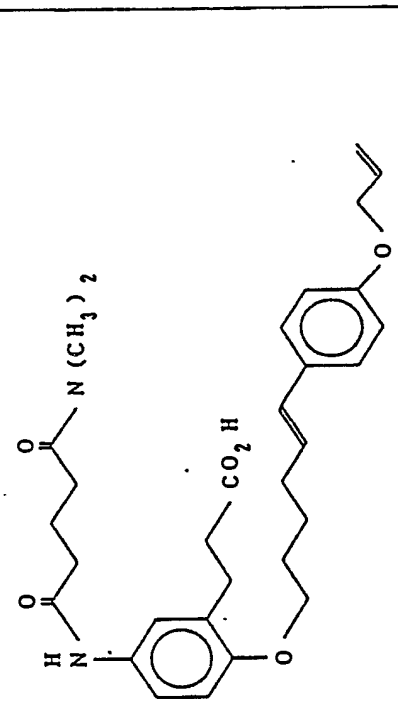
Ex.No.	Structural formula	T L C	I R (cm^{-1})
1 (e)		Rf 0.30 (chloroform: methanol = 10:1)	ν 1634. 1506. 1242. 1048. 977. 810
1 (f)		Rf 0.28 (chloroform: methanol = 10:1)	ν 2937. 1715. 1607. 1550 1505. 1472. 1422. 1240. 1176. 1119. 1023. 969. 810. 756

Table 4 (continued)

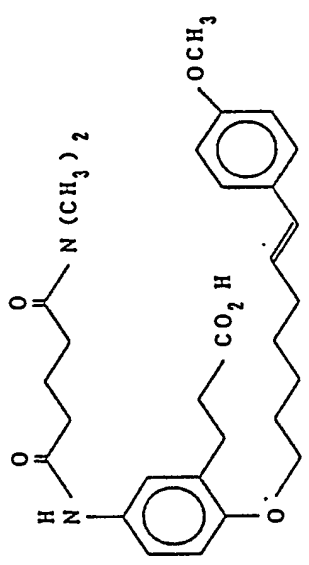
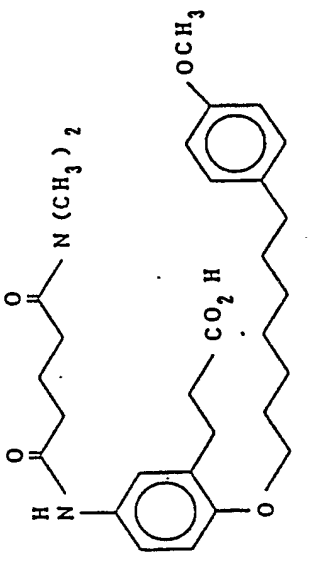
Ex.No.	Structural formula	T L C	I R (cm^{-1})
1 (g)		Rf 0.30 (ethyl acetate: methanol = 6:1)	ν 3273. 2932. 2855. 2837. 1711. 1650. 1601. 1540. 1511. 1406. 1416. 1348. 1248. 1229. 1178. 1116. 1034. 971. 805
1 (h)		Rf 0.30 (ethyl acetate: methanol = 6:1)	ν 3284. 3067. 2927. 2854. 1735. 1711. 1650. 1624. 1600. 1561. 1511. 1468. 1416. 1246. 1172. 1117. 1033. 805

Table 4 (continued)

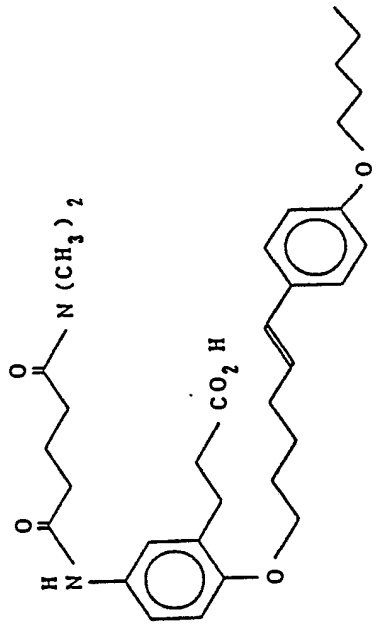
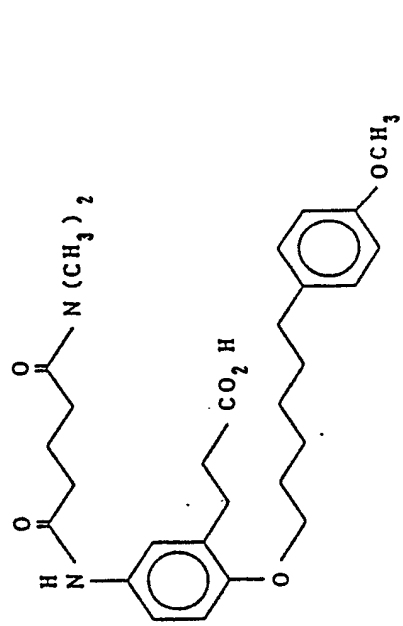
Ex.No.	Structural formula	T L C	I R (cm^{-1})
1 (i)		Rf 0.27 (chloroform: methanol =10:1)	ν 3305. 2933. 1728. 1608. 1550. 1504. 1471. 1242. 1175. 1119. 1051. 968. 810. 756
1 (j)		Rf 0.49 (ethyl acetate: methanol =6:1)	ν 3304. 2933. 2857. 1727. 1613. 1548. 1512. 1504. 1469. 1419. 1245. 1178. 1118. 1036. 883. 813. 753

Table 4 (continued)

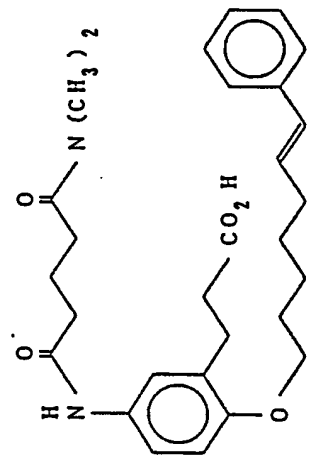
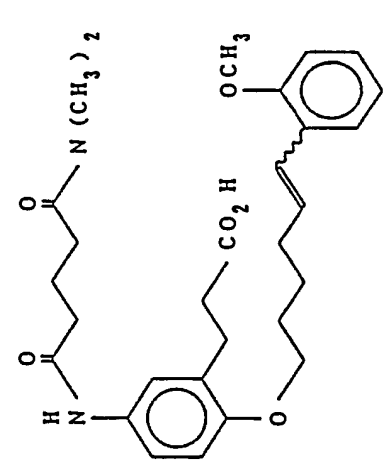
Ex.No.	Structural formula	T L C	I R (cm^{-1})
1 (k)		R f 0.49 (ethyl acetate: methanol = 6:1)	ν 3276. 2933. 1710. 1648. 1600. 1539. 1503. 1414. 1347. 1258. 1228. 1116. 1058. 968. 883. 805. 694
1 (ℓ)		R f 0.34 (ethyl acetate: methanol = 6:1)	ν 3300. 2937. 1719. 1616. 1549. 1503. 1467. 1438. 1420. 1242. 1162. 1118. 1051. 1029. 976. 884. 814

Table 4 (continued)

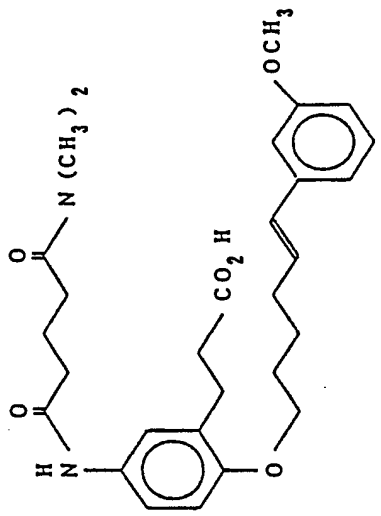
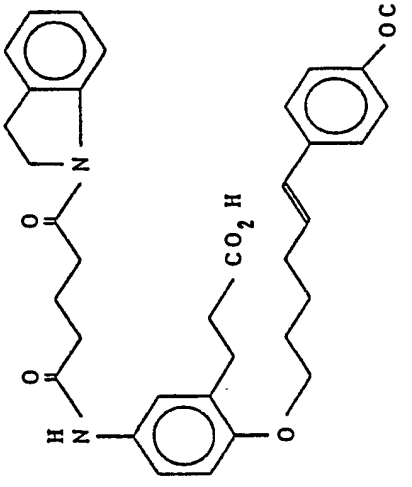
Ex.No.	Structural formula	T L C	I R (cm^{-1})
1 (m)		Rf 0.39 (ethyl acetate: methanol = 6:1)	ν 3301. 3008. 2938. 1723. 1607. 1549. 1503. 1471. 1453. 1423. 1236. 1156. 1119. 1047. 971. 881. 813. 756
1 (n)		Rf 0.50 (ethyl acetate: methanol = 10:1)	ν 2936. 1273. 1655. 1510. 1484. 1420. 1246

Table 4 (continued)

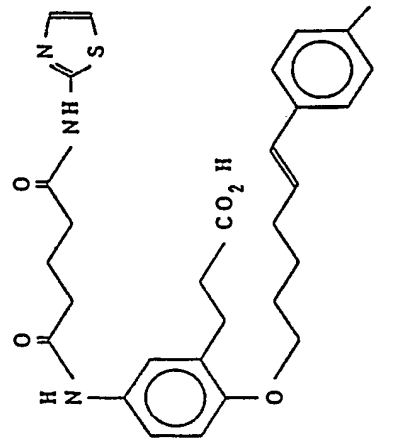
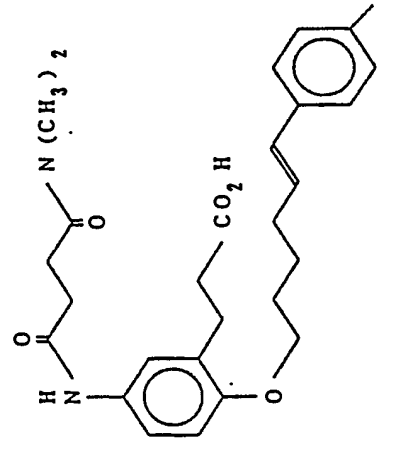
Ex.No.	Structural formula	T L C	I R (cm^{-1})
1 (o)		Rf 0.40 (ethyl acetate: methanol = 10:1)	ν 3273. 2933. 1691. 1646. 1551. 1511. 1248
1 (p)		Rf 0.55 (ethyl acetate: methanol = 6:1)	ν 3295. 3262. 2936. 1695. 1676. 1609. 1552. 1511. 1501. 1474. 1275. 1245. 1116. 1031. 972. 882. 842. 816

Table 4 (continued)

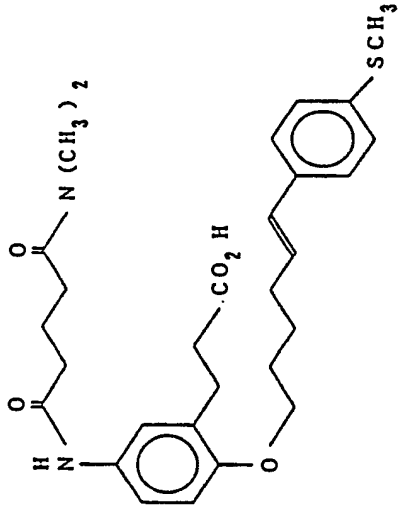
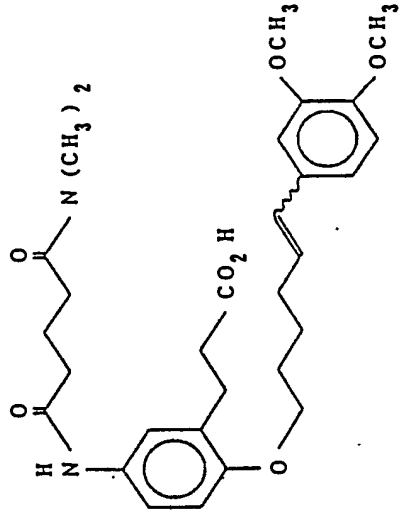
Ex.No.	Structural formula	T L C	I R (cm^{-1})
1 (q)		Rf 0.29 (ethyl acetate: methanol = 6:1)	ν 3283. 3120. 2934. 2864. 1732. 1650. 1623. 1526. 1500. 1475. 1459. 1439. 1416. 1347. 1233. 1175. 1117. 969. 802
1 (r)		Rf 0.24 (ethyl acetate: methanol = 6:1)	ν 3303. 3010. 2936. 1770. 1725. 1625. 1549. 1514. 1501. 1467. 1418. 1262. 1236. 1140. 1119. 1027. 755

Table 4 (continued)

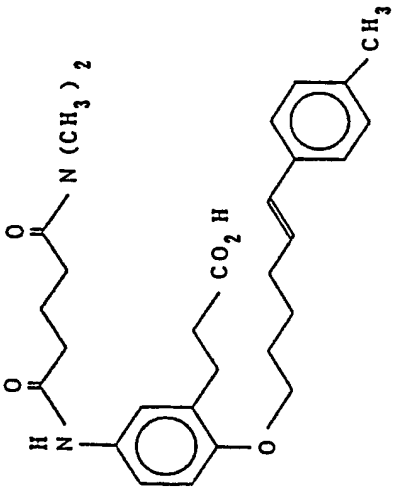
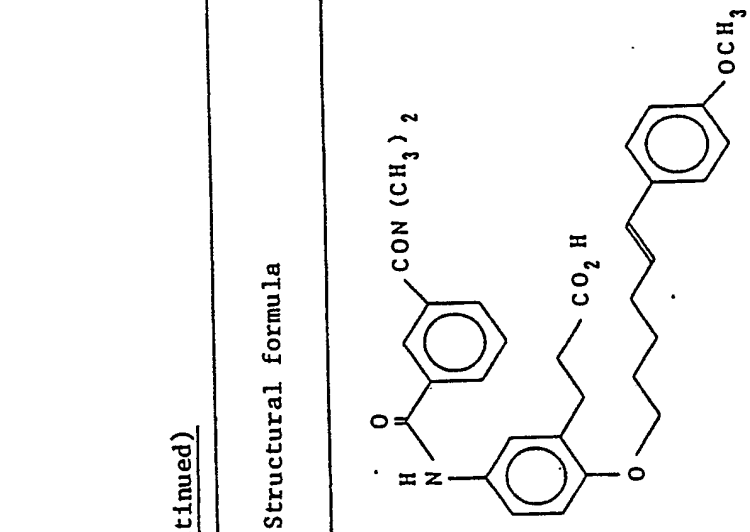
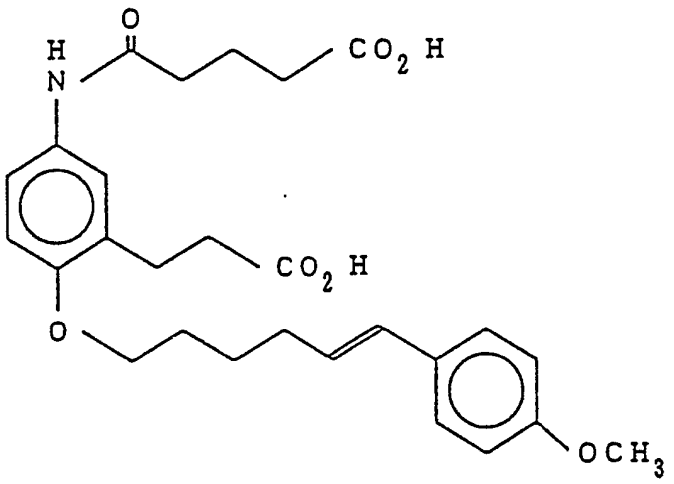
Ex.No.	Structural formula	T L C	I R (cm^{-1})
1 (s)		Rf 0.36 (ethyl acetate: methanol = 6:1)	ν 3301. 3011. 2937. 2869. 1723. 1616. 1549. 1504. 1472. 1414. 1235. 1119. 1043. 969. 813. 756
1 (t)		Rf 0.40 (ethyl acetate: methanol = 6:1)	ν 3300. 3011. 2937. 1714. 1615. 1549. 1503. 1472. 1405. 1234. 1119. 1091. 1013. 969. 811. 756

Table 4 (continued)

Ex.No.	Structural formula	T L C	I R (cm^{-1})
1 (u)		Rf 0.40 (ethyl acetate: methanol = 10:1)	ν 3350. 2934. 1724. 1611. 1510. 1249

Example 2

3-[1-[6-(4-methoxyphenyl)hex-5E-enyl]oxy-4-(4-carboxylbutanamido)benzen-2-yl]propionic acid

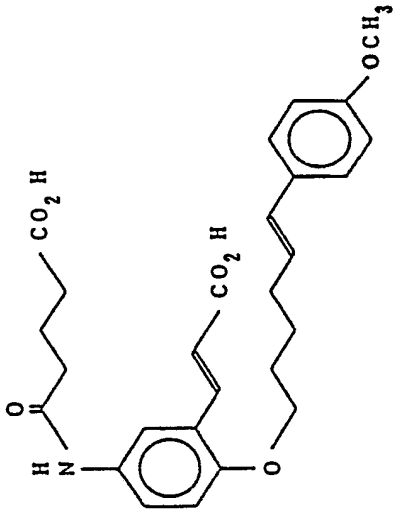
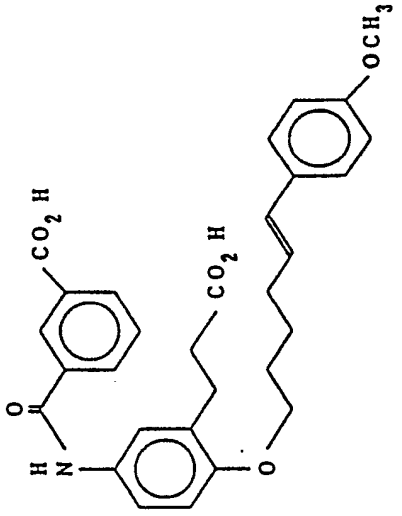


The title compound, of the present invention, having the following physical data was obtained with using the ester prepared in reference example 5 by the same procedure as example 1.
TLC(chloroform : methanol : acetic acid = 17 : 2 : 1) : Rf 0.70;
IR(cm-1) : ν 3276, 2932, 1702, 1650, 1609, 1541, 1512, 1245, 1223.

Example 2(a) and 2(b)

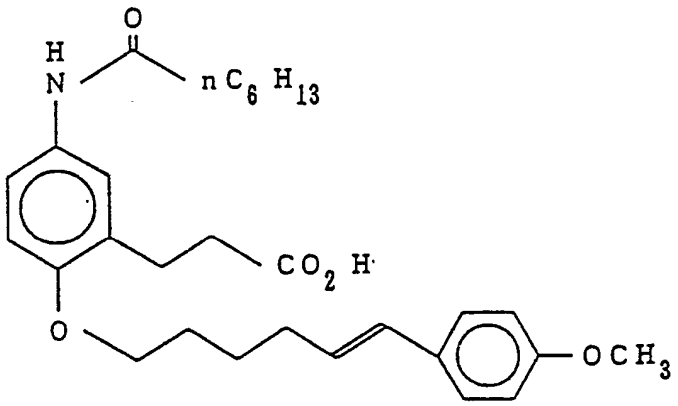
The compounds, of the present invention, shown in the following table 5 were obtained, with using a tert-butyl ester, which was prepared with using the ester prepared in reference example 9 by the same procedure as reference example 4 → reference example 5, for example 2(a), and a tert-butyl ester, which was prepared with using the compound prepared in reference example 2 by the same procedure as reference example 3 (with the proviso that 3-carboxylbenzoyl chloride was used instead of 4-methoxycarbonylbutanoylchloride) → reference example 4 → reference example 5, for example 2(b), by the same procedure as example 2.

Table 5

Ex.No.	Structural formula	T L C	I R (cm^{-1})
2 (a)		Rf 0.40 (chloroform: methanol = 100:10:1)	ν 3294. 2935. 1699. 1665. 1626. 1513. 1418. 1247. 962
2 (b)		Rf 0.70 (chloroform: methanol =)	ν 3281. 2935. 1702. 1643. 1608. 1536. 1510. 1247

Example 3

3-[1-[6-(4-methoxyphenyl)hex-5E-enyl]oxy-4-heptanamidobenzen-2-yl]propionic acid



The title compound of the present invention, having the following physical data, was obtained with using the compound, which was prepared with using the ester prepared in reference example 2 by the same procedure as reference example 3 (with the proviso that heptanoyl chloride was used instead of methyl 4-(chloroformyl)butyrate) → reference example 4, by the same procedure as example 1.
TLC(ethyl acetate) : Rf 0.40;
IR(cm^{-1}) : ν 3436, 3269, 2934, 2872, 1732, 1607, 1559, 1512, 1252.

Example 3(a) - 3(c)

The compounds, of the present invention, shown in the following table 6 was obtained with using the corresponding acyl halide instead of heptanoyl chloride by the same procedure as example 3.

Table 6

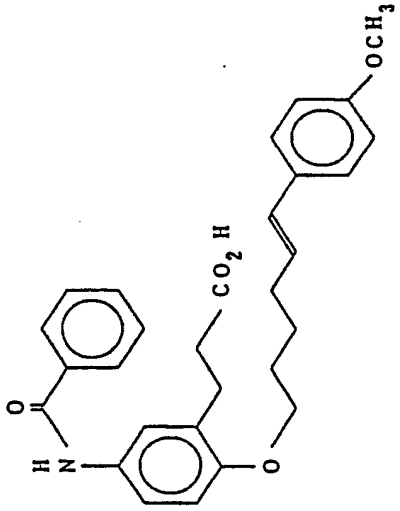
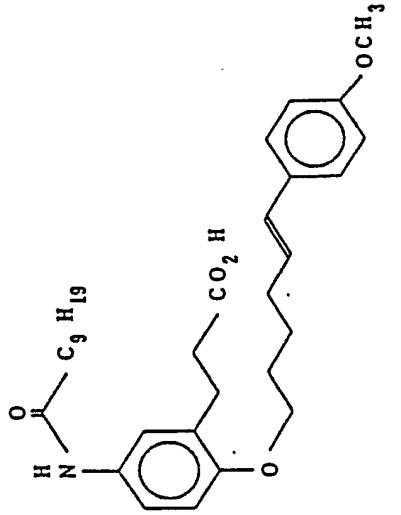
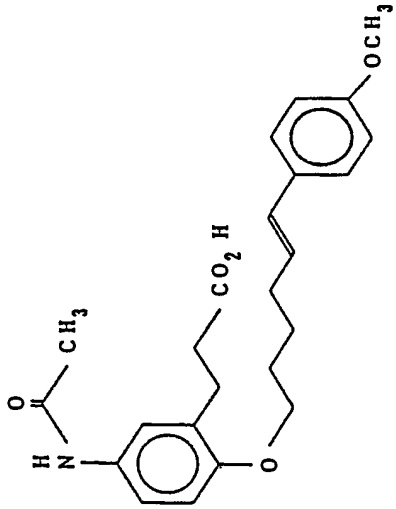
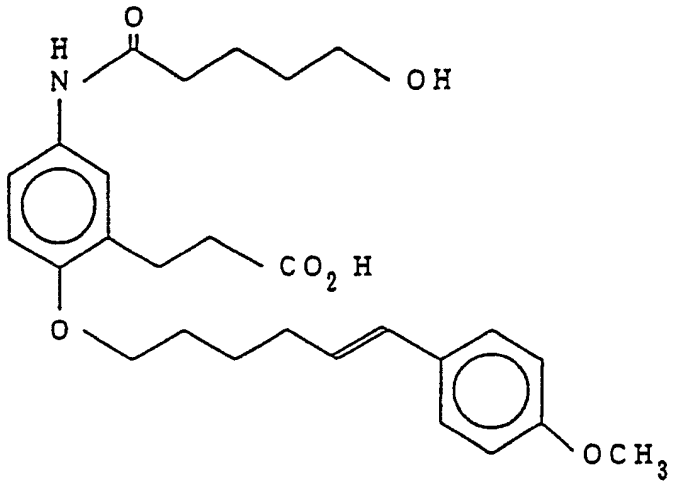
Ex.No.	Structural formula	T L C	I R (cm^{-1})
3 (a)		R f 0.60 (ethyl acetate)	ν 3277. 2935. 1698. 1643. 1608. 1533. 1510. 1248
3 (b)		R f 0.50 (ethyl acetate)	ν 3281. 2922. 2852. 1698. 1651. 1609. 1541. 1511. 1250

Table 6 (continued)

Ex.No.	Structural formula	T L C	I R (cm^{-1})
3 (c)		R f 0.40 (ethyl acetate: methanol =10:1)	ν 3326. 2940. 1709. 1636. 1609. 1561. 1510. 1248

Example 4

3-[1-[6-(4-methoxyphenyl)hex-5E-enyl]oxy-4-(5-hydroxypentanamido)benzen-2-yl]propionic acid

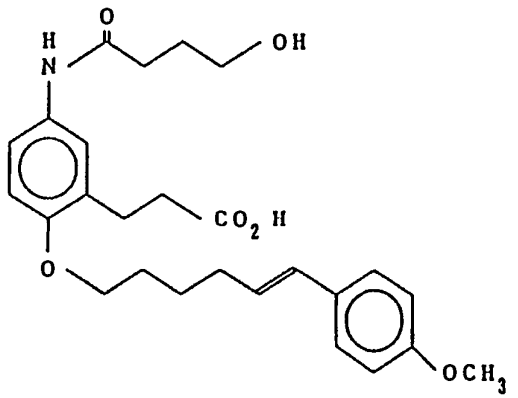
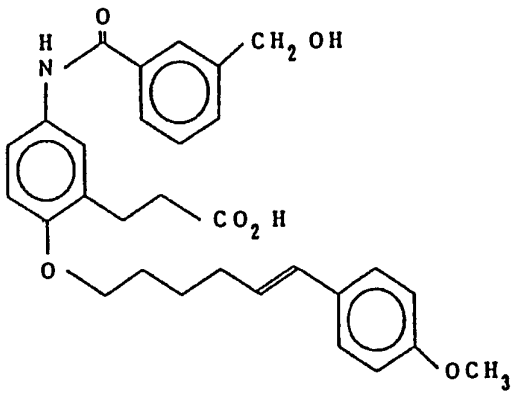


The title compound, of the present invention, having the following physical data was obtained with using the ester prepared in reference example 7, by the same procedure as example 1.
TLC(ethyl acetate : methanol = 7 : 1) : Rf 0.50;
MS : m/z 469(M^+), 369, 189, 163, 147, 121.

Example 4(a) and 4(b)

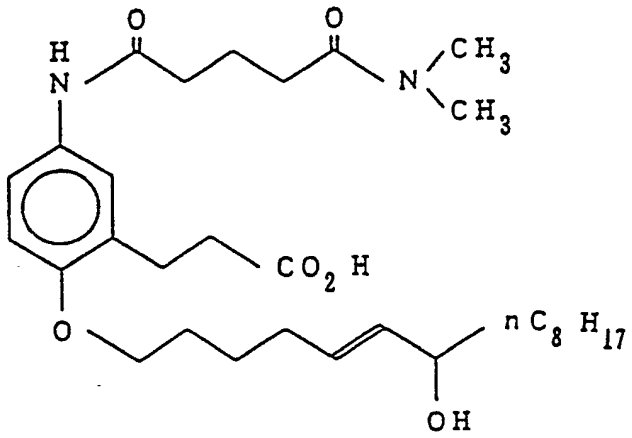
The compounds, of the present invention, shown in the following table 7 were obtained, with using a tert-butyl ester, which was prepared with using the tert-butyl ester prepared in reference example 2 by the same procedure as reference example 3 (with the proviso that the corresponding appropriate reagents were used instead of 4-methoxycarbonylbutanoyl chloride) → reference example 4 → reference example 5 → reference example 7, by the same procedure example 4.

Table 7

Ex.No.	Structural formula	T L C	I R (cm^{-1})
4 (a)		R f 0.67 (ethyl acetate: methanol -6:1)	ν 3288. 2944. 2837. 2529. 1698. 1663. 1607. 1555. 1509. 1473. 1443. 1339. 1278. 1246. 1235. 1176. 1159. 1111. 1033. 971. 834
4 (b)		R f 0.50 (ethyl acetate: methanol -10:1)	ν 3368. 2932. 1731. 1642. 1607. 1541. 1508. 1245. 1176. 1033

Example 5

3-[1-(5E-7-hydroxypentadecenyl)oxy-4-(4-dimethylaminocarbonylbutanamido)benzen-2-yl]propionic acid



The title compound, of the present invention, having the following physical data was obtained with using the methyl ester prepared in reference example 16 by the same procedure as reference example 5.
TLC(chloroform : methanol = 10 : 1) : Rf 0.29;
IR(cm^{-1}) : ν 3306, 2928, 2856, 1712, 1626, 1552, 1504, 1470, 1414, 1235, 1119, 1051, 972, 812.

Example 5(a) - 5(e)

The compounds, of the present invention, shown in the following table 8 were obtained with using the compounds, which were prepared with using the corresponding appropriate reagent by the same procedure as the steps for the preparation of the compound of reference example 16, by the same procedure as example 5.

Table 8

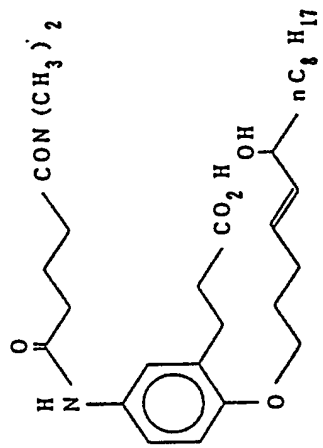
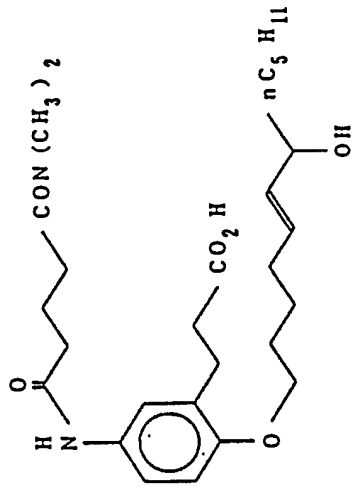
Ex.No.	Structural formula	T L C	I R (cm^{-1})
5 (a)		Rf 0.35 (chloroform: methanol = 10:1)	ν 532 (M^+), 514, 391
5 (b)		Rf 0.29 (chloroform: methanol = 10:1)	ν 3304, 2932, 2859, 1718, 1626, 1551, 1504, 1471, 1407, 1235, 1119, 1052, 972, 912, 885, 813, 733

Table 8 (continued)

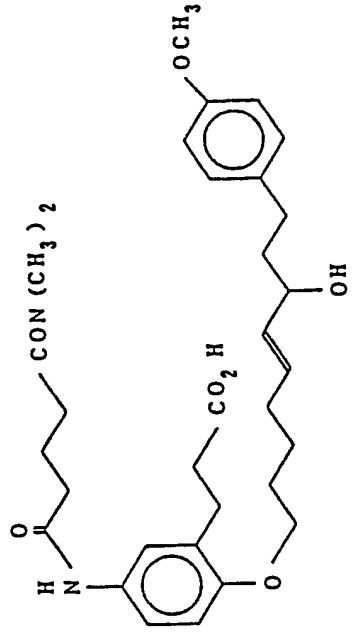
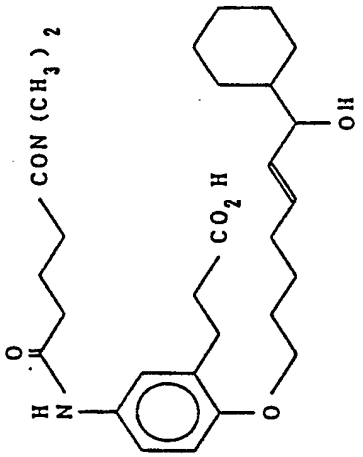
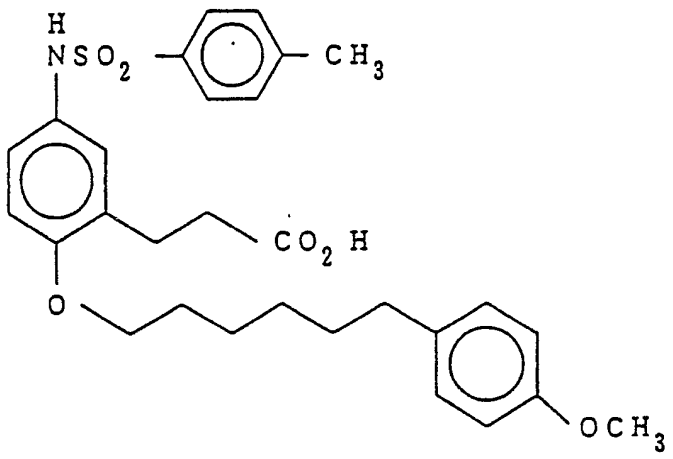
Ex.No.	Structural formula	T L C	I R (cm^{-1})
5 (c)		Rf 0.28 (chloroform: methanol = 10:1)	ν 3305. 2937. 2863. 1718. 1614. 1549. 1512. 1504. 1471. 1419. 1246. 1179. 1119. 1038. 973. 815. 755. 666
5 (d)		Rf 0.28 (chloroform: methanol = 10:1)	ν 3305. 2934. 2874. 1723. 1658. 1615. 1550. 1504. 1471. 1416. 1235. 1119. 1049. 972. 813. 733

Table 8 (continued)

Ex.No.	Structural formula	T L C	I R (cm^{-1})
5 (e)		Rf 0.28 (chloroform: methanol = 10:1)	ν 3305. 2927. 2854. 1714. 1626. 1551. 1504. 1473. 1450. 1417. 1235. 1119. 1044. 974. 913. 892. 813. 733

Example 6

3-[1-[6-(4-methoxyphenyl)hexyl]oxy-4-(4-methylphenyl)sulfonylaminobenzen-2-yl]propionic acid



The title compound, of the present invention, having the following physical data was obtained with using a tert-butyl ester, which was prepared with using the tert-butyl ester prepared in reference example 17 by the same procedure as reference example 4 (with the proviso that the corresponding appropriate methanesulfonate was used instead of 6-(p-methoxyphenyl)-5E-hexenol methanesulfonate) → reference example 18 → reference example 3 (with the proviso that the corresponding appropriate sulfonyl chloride was used instead of 4-methoxycarbonylbutanoyl chloride), by the same procedure as example 1.
TLC(ethyl acetate : n-hexane = 2 : 1) : Rf 0.40;
IR(cm^{-1}) : ν 3256, 2932, 2857, 1714, 1612, 1505, 1471, 1396, 1245, 1158, 1037, 815, 667.

Example 6(a) - 6(c)

The compounds, of the present invention, shown in the following table 9 were obtained by the same procedure as example 6.

Table 9

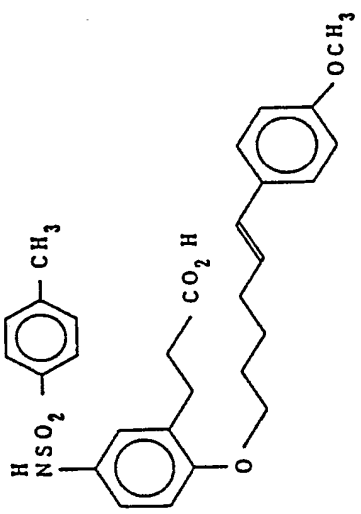
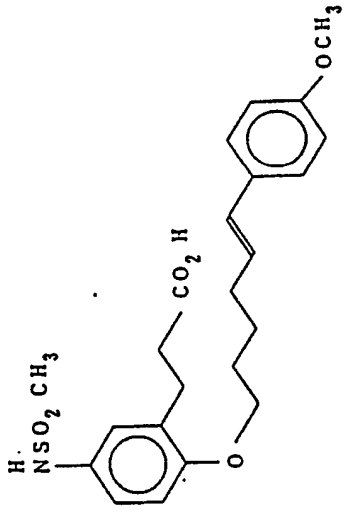
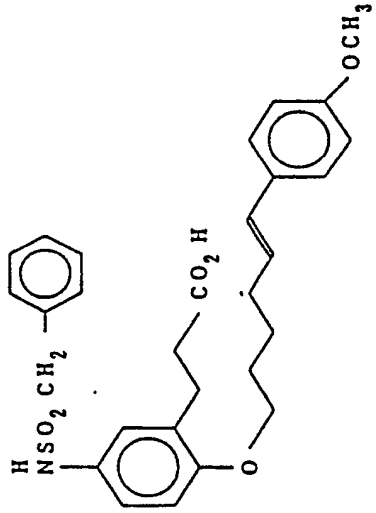
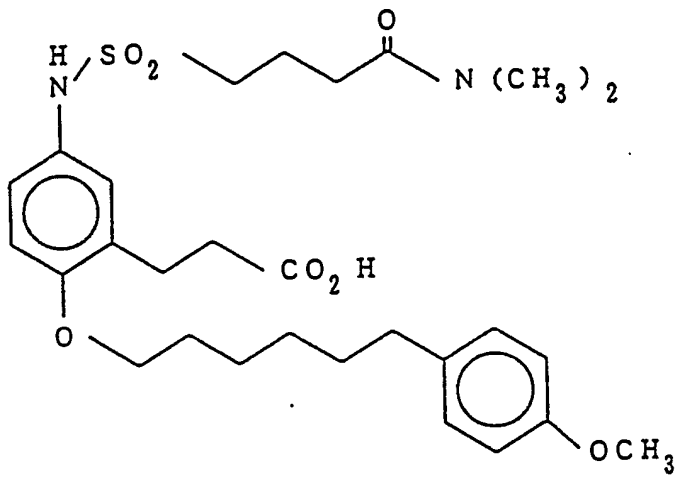
Ex.No.	Structural formula	T L C	I R (cm^{-1})
6 (a)		R f 0.30 (ethyl acetate: n-hexane = 2:1)	ν 3264. 2936. 1708. 1608. 1511. 1248. 1160
6 (b)		R f 0.30 (ethyl acetate)	ν 3259. 2935. 1697. 1511. 1311. 1249. 1225. 1152

Table 9 (continued)

Ex.No.	Structural formula	T L C	I R (cm^{-1})
6 (c)		Rf 0.30 (ethyl acetate: n-hexane = 2:1)	ν 3247. 2935. 1708. 1510. 1247. 1154

Example 7

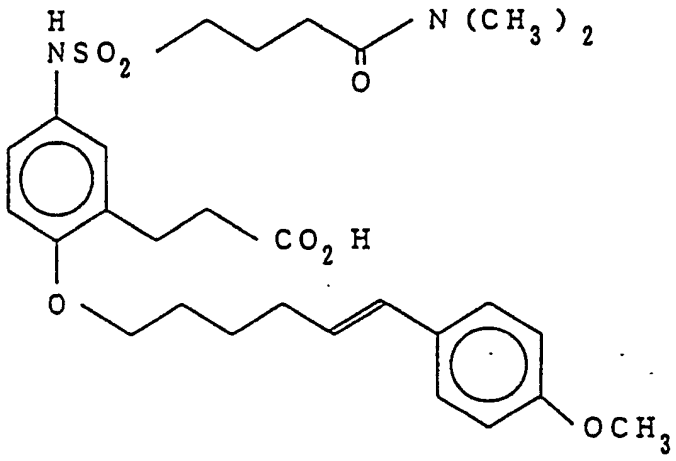
3-[1-[6-(4-methoxyphenyl)hexyl]oxy-4-(3-dimethylaminocarbonyl-n-propyl)sulfonylaminobenzen-2-yl]-propionic acid



The title compound, of the present invention, having the following physical data was obtained with using the phenol compound (prepared in reference example 1) by the same procedure as reference example 4 (with the proviso that the corresponding appropriate methanesulfonate was used instead of 6-(p-methoxyphenyl)-5E-hexenol methanesulfonate) → reference example 2 → reference example 3 (with the proviso that the corresponding appropriate sulfonyl chloride was used instead of 4-methoxycarbonylbutanoyl chloride) → reference example 5 → reference example 6 → example 1.
TLC(ethyl acetate) : Rf 0.10;
IR(cm^{-1}) :ν 2933, 1693, 1621, 1512, 1247, 1207, 1148.

Example 7(a)

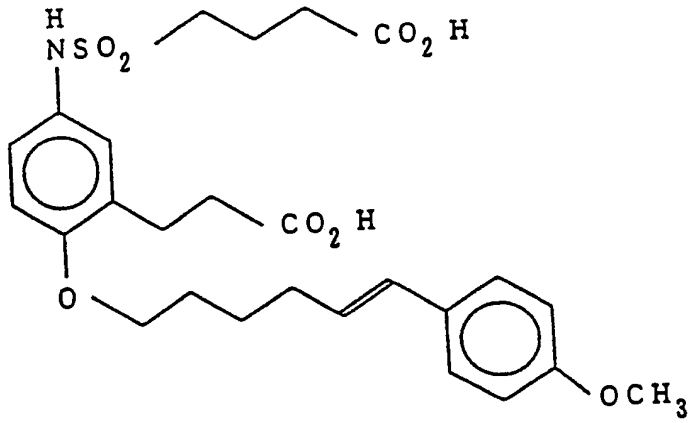
3-[1-[6-(4-methoxyphenyl)hex-5E-enyl]oxy-4-(3-dimethylaminocarbonyl-n-propyl)sulfonylaminobenzen-2-yl]-propionic acid



The title compound, of the present invention, having the following physical data was obtained by the same procedure as example 7.
TLC(ethyl acetate : methanol = 10 : 1) : Rf 0.30;
IR(cm^{-1}) :ν 2937, 1732, 1615, 1505, 1246, 1152, 1034.

Example 8

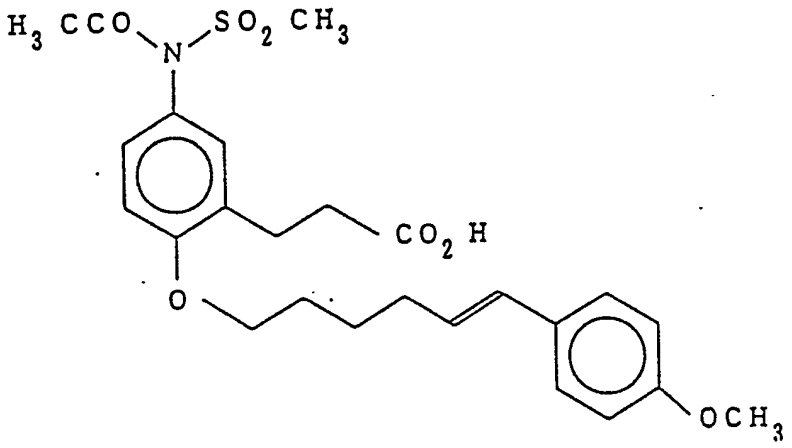
3-[1-[6-(4-methoxyphenyl)hex-5E-enyl]oxy-4-(3-carboxylpropyl)sulfonylaminobenzen-2-yl]propionic acid



The title compound, of the present invention, having the following physical data was obtained with using the tert-butyl ester prepared in reference example 18 by the same procedure as reference example 3 → reference example 5 → example 1. TLC(ethyl acetate : methanol = 9 : 1) : Rf 0.10;
IR(cm^{-1}) :ν 3270, 2932, 1713, 1608, 1504, 1470, 1299, 1153.

Example 9

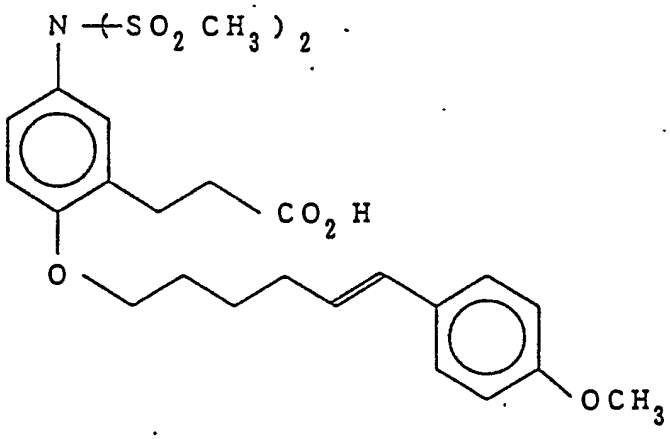
3-[1-[6-(4-methoxyphenyl)hex-5E-enyl]oxy-4-(N-acetyl-N-mesyl)-aminobenzen-2-yl]propionic acid



The title compound, of the present invention, having the following physical data was obtained with using the tert-butyl ester prepared in reference example 19 by the same procedure as example 1.
TLC(ethyl acetate) : Rf 0.30;
IR(cm^{-1}) :ν 2937, 1707, 1511, 1500, 1353, 1246, 1163.

Example 10

3-[1 [6-(4-methoxyphenyl)hex-5E-enyl]oxy-4-dimesylaminobenzen-2-yl]propionic acid



The title compound, of the present invention, having the following physical data was obtained with using the tert-butyl ester prepared in reference example 20 by the same procedure as example 1.
TLC(ethyl acetate : n-hexane = 2 ; 1) : Rf 0.25;
IR(cm^{-1}) :ν 2936, 1708, 1607, 1511, 1368,, 1248, 1161.

Example 10(a) - 10(c)

The compounds, of the present invention, shown in the following table 10 were obtained with using tert-butyl esters, which were prepared with using the ester prepared in reference example 18 by the same procedure as reference example 20 (with the proviso that the corresponding appropriate sulfonyl chloride was used instead of methanesulfonyl chloride), by the same procedure as example 10.

Table 10

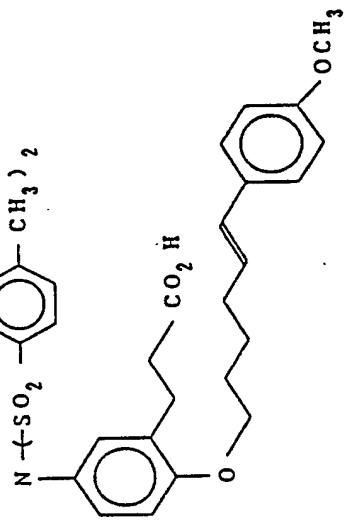
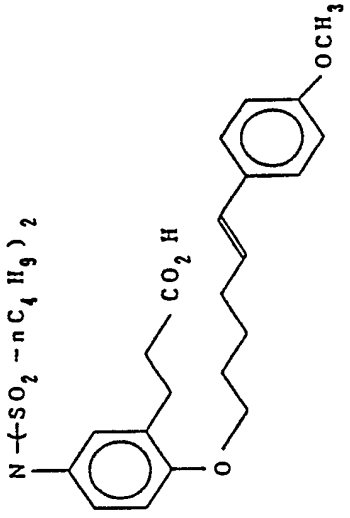
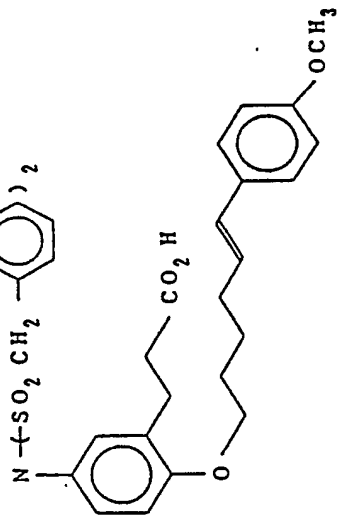
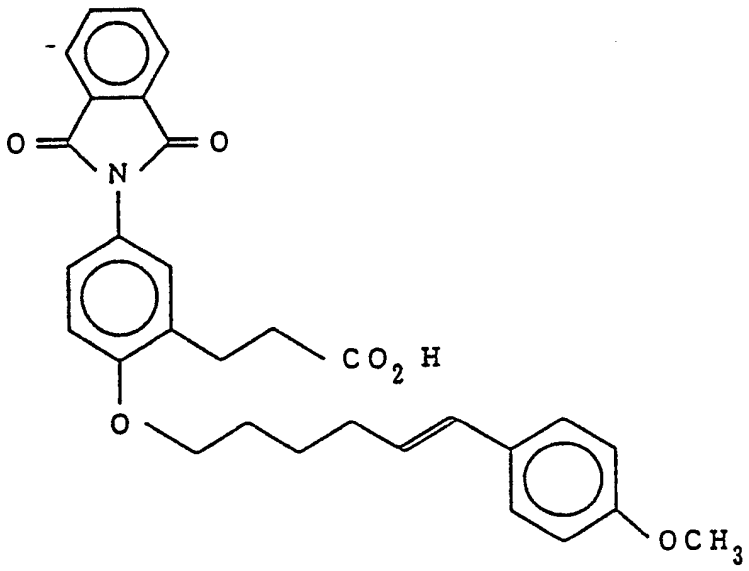
Ex.No.	Structural formula	T L C	I R (cm^{-1})
10 (a)		Rf 0.30 (ethyl acetate: n-hexane = 2:1)	ν 2934. 1709. 1607. 1511. 1499. 1377. 1249. 1168. 662. 549
10 (b)		Rf 0.40 (ethyl acetate: n-hexane = 2:1)	ν 2961. 1714. 1607. 1504. 1470. 1380. 1036. 914. 865

Table 10 (continued)

Ex.No.	Structural formula	T L C	I R (cm^{-1})
10 (c)		R f 0.40 (ethyl acetate: n-hexane =2:1)	ν : 2932. 1708. 1607. 1511. 1498. 1374. 1352. 1249. 1158

Example 11

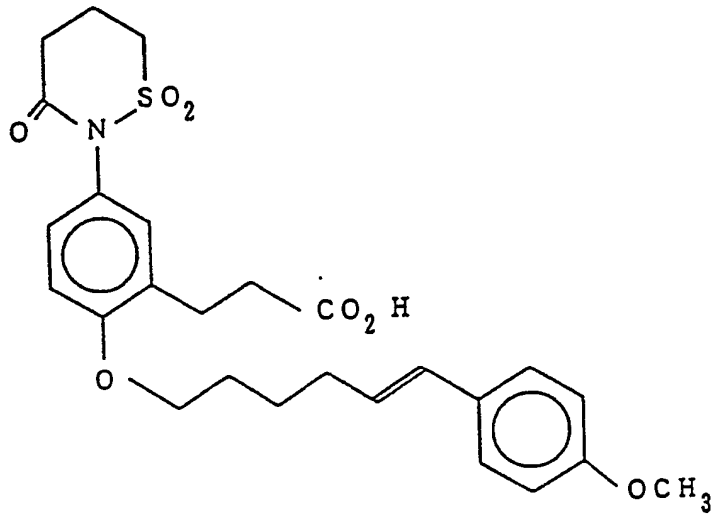
3-[1-[6-(4-methoxyphenyl)hex-5E-enyl]oxy-4-phthalimidobenzen-2-yl]propionic acid



The title compound, of the present invention, having the following physical data was obtained with using the tert-butyl ester prepared in reference example 21 by the same procedure as example 1.
MS : m/z 499 (M^+), 293, 265, 189, 147, 121;
IR(cm^{-1}) : ν 3215, 2935, 1756, 1702. 1511, 1256, 1150, 1122, 725.

Example 12

3-[1-[6-(4-methoxyphenyl)hex-5E-enyl]oxy-4-(perhydro-1,2-thiazin-1,1,3-trione-2-yl]benzen-2-yl]propionic acid

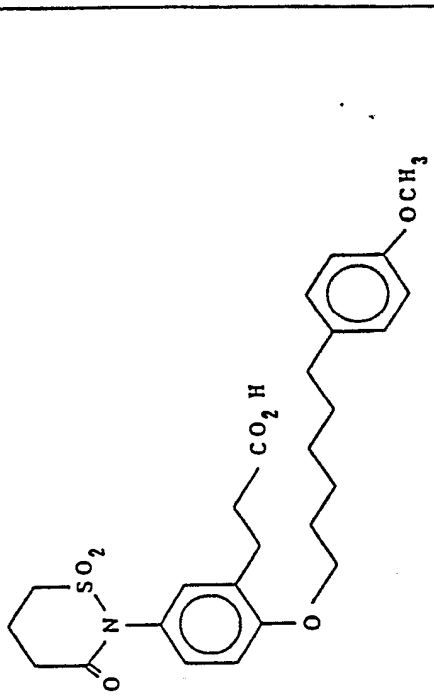
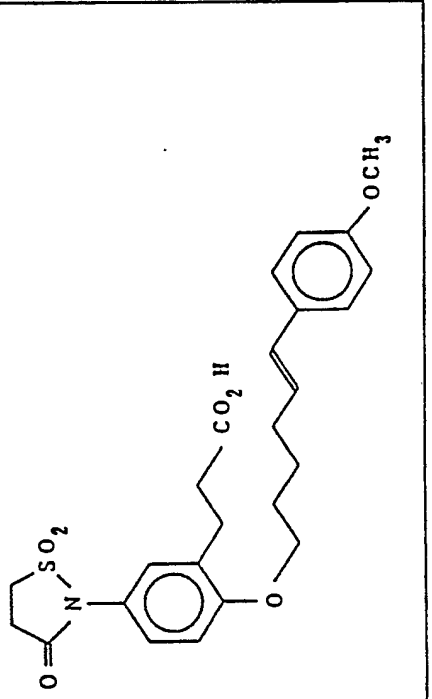


The title compound, of the present invention, having the following physical data was obtained with using the tert-butyl ester prepared in reference example 22 by the same procedure as example 1.
TLC(ethyl acetate : methanol = 10 . 1) : Rf 0.40;
IR(cm-1) :ν 2935, 1718, 1697, 1511, 1500, 1333, 1248, 1151, 1120, 1025.

Example 12(a) and 12(b)

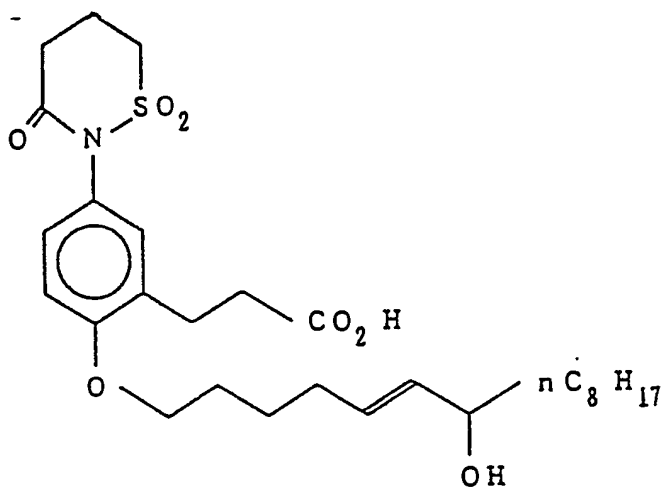
The compounds, of the present invention, shown in the following table 11 were obtained with using the compounds, which were prepared with using the corresponding appropriate reagents by the same procedure as the steps for the preparation of the compound of reference example 22, by the same procedure as example 12.

Table 11

Ex.No.	Structural formula	T L C	I R (cm^{-1})
12 (a)		R f 0.20 (ethyl acetate)	ν 2933. 1717. 1696. 1513. 1500. 1333. 1249. 1152. 1121. 1026. 821. 529
12 (b)		R f 0.40 (ethyl acetate: methanol =10:1)	ν 3362. 1729. 1510. 1323. 1250. 1159

Example 13

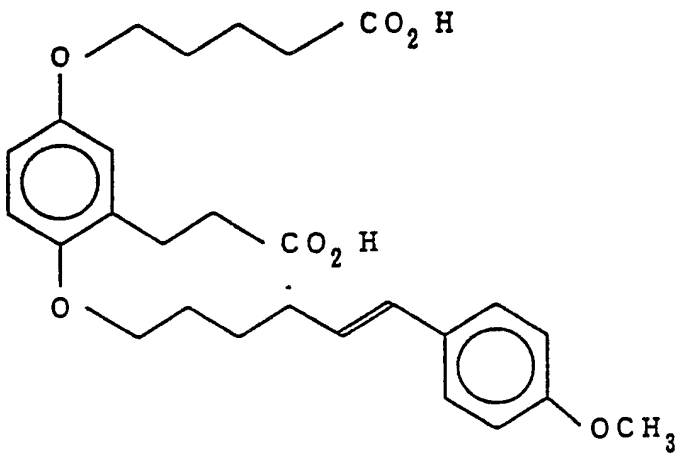
3-[1-(5E-7-hydroxy-n-pentadecenyl)oxy-4-(perhydro-1,2-thiazin-1,1,3-trione-2-yl)benzen-2-yl]propionic acid



The title compound, of the present invention, having the following physical data was obtained with using the tert-butyl ester prepared in reference example 23 by the same procedure as reference example 14 → reference example 15 → reference example 16 → reference example 18 → reference example 3 (with the proviso that the corresponding appropriate sulfonyl chloride was used instead of 4-methoxycarbonylbutanoyl chloride) → reference example 5 → reference example 22 → reference example 11 → reference example 13.
TLC(ethyl acetate : methanol = 9 : 1) : Rf 0.50;
MS : m/z 537 (M^+), 519, 424, 406, 369, 342, 313, 295.

Example 14

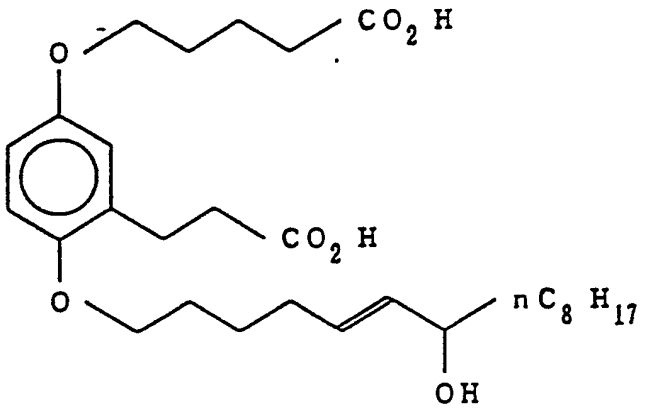
3-[1-[6-(4-methoxyphenyl)hex-5E-enyl]oxy-4-(4-carboxylbutoxy)benzen-2-yl]propionic acid



The title compound, of the present invention, having the following physical data was obtained with using the ethyl ester prepared in reference example 27 by the same procedure as reference example 2 → reference example 4 → reference example 5 and then purification by column chromatography on silica gel.
TLC(chloroform : methanol = 10 : 1) : Rf 0.35;
IR(cm^{-1}) : ν 2938, 1669, 1606, 1510, 1474, 1426, 1289, 1246, 1227, 1178, 1109, 1053, 968, 847, 805.

Example 15

3-[1-(5E-7-hydroxy-n-pentadecenyl)oxy-4-(4carboxylbutyl)-oxybenzen-2-yl]propionic acid



The title compound, of the present invention, having the following physical data was obtained with using the ethyl ester prepared in reference example 27 by the same procedure as reference example 2 → reference example 10 → reference example 23 → reference example 14 → reference example 15 → reference example 16 → reference example 5 and then purification by column chromatography on silica gel.
TLC(chloroform : methanol) : Rf 0.36;
IR(cm^{-1}) :ν 2926, 2852, 1696, 1508, 1466, 1278, 1229, 1168, 1108, 1070, 972, 873, 810.

Example 15(a) - 15(c)

The compounds, of the present invention, shown in the following table 12 were obtained with using 6-

hydroxycoumarin prepared in reference example 25 by the same procedure as reference example 26 (with the proviso that the corresponding appropriate esters were used instead of ethyl 5-bromopentanoate in example 15(b) and 15(c)) → reference example 27 → reference example 2 → reference example 10 → reference example 23 → reference example 14 → reference example 15 (with the proviso that the corresponding appropriate phosphonate was used instead of dimethyl 2-oxodecylphosphonate for example 15(a)) → reference example 16 → reference example 5 and then purification by column chromatography on silica gel.

Table 12

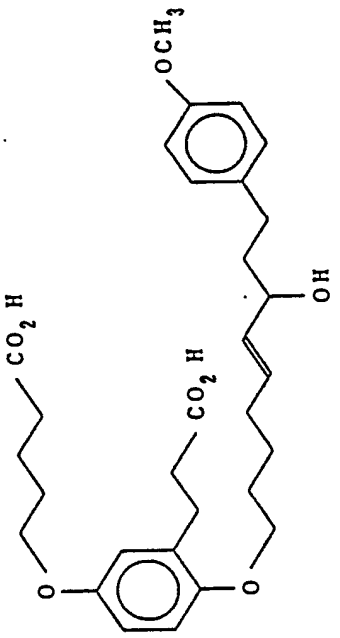
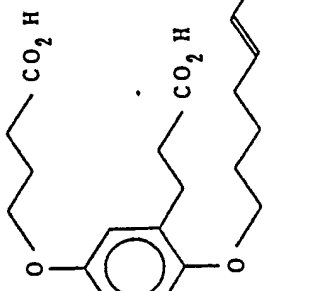
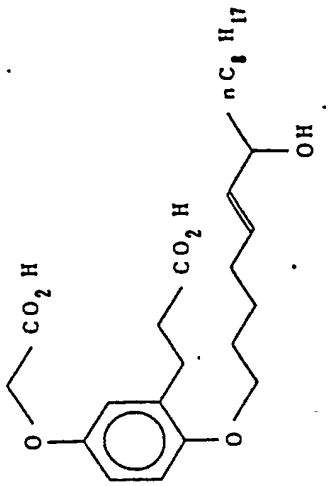
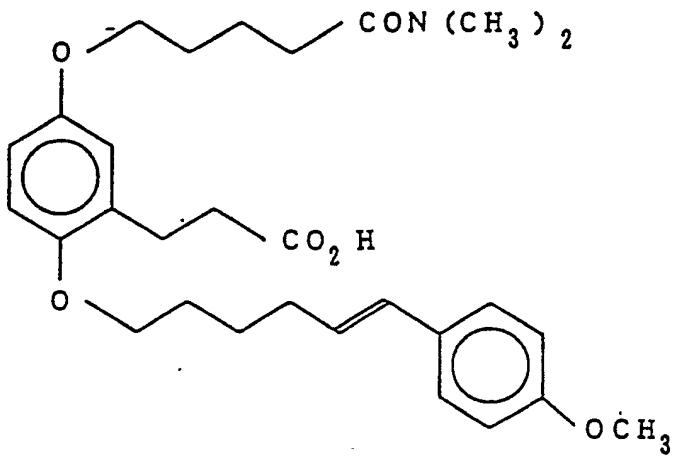
Ex.No.	Structural formula	T L C	I R (cm^{-1})
15 (a)		Rf 0.26 (chloroform: methanol = 10:1)	ν 2937. 1709. 1612. 1586. 1513. 1501. 1470. 1246. 1221. 1178. 1038. 974. 810. 758
15 (b)		Rf 0.25 (chloroform: methanol = 10:1)	ν 3531. 2925. 2852. 1694. 1507. 1466. 1426. 1406. 1393. 1300. 1258. 1228. 1208. 1167. 1110. 1060. 1022. 977. 897. 868. 816. 807. 712

Table 12 (continued)

Ex.No.	Structural formula	T L C	I R (cm^{-1})
15 (c)		Rf 0.09 (chloroform: methanol = 10:1)	ν 3419. 3138. 2926. 2853. 1725. 1594. 1500. 1441. 1420. 1404. 1253. 1222. 1181. 1123. 1090. 978. 952. 879. 777

Example 16

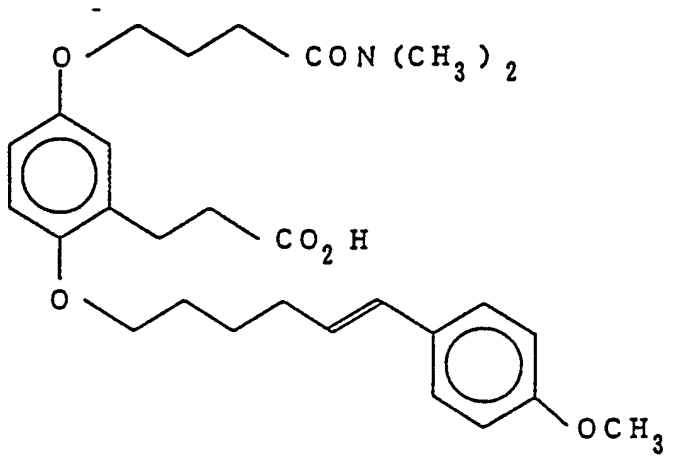
3-[1-[6-(4-methoxyphenyl)hex-5E-enyl]oxy-4-(4-dimethylaminocarbonyl-n-butyl)oxybenzen-2-yl]propionic acid



The title compound, of the present invention, having the following physical data was obtained with using 6-hydroxy-coumarin prepared in reference example 25 by the same procedure as reference example 26 (with the proviso that N,N-dimethyl-5-bromopentanamide was used instead of ethyl 5-bromopentanoate) → reference example 27 → reference example 2→ reference example 4 → reference example 5 and then purification by column chromatography on silica gel.
TLC(chloroform : methanol = 10 : 1) : Rf 0.56;
IR (cm^{-1}) ;ν 2937, 1728, 1609, 1510, 1411, 1402, 1247, 1220, 1176, 1121, 1036, 969, 846, 803, 756.

Example 16(a)

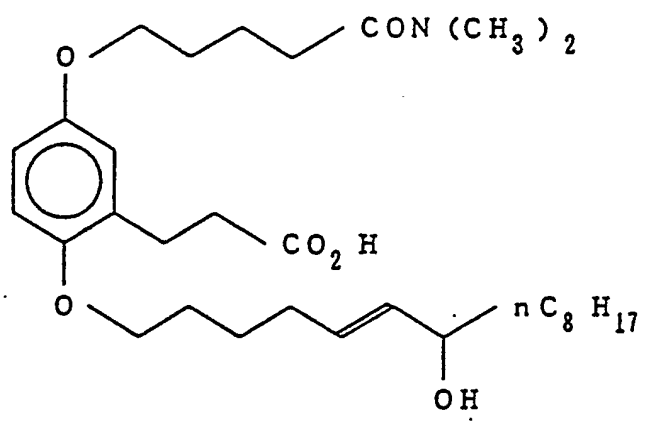
3-[1-[6-(4-methoxyphenyl)hex-5E-enyl]oxy-4-(3-dimethylaminocarbonyl-n-propyl)oxybenzen-2-yl]propionic acid



The title compound, of the present invention, having the following physical data was obtained with using 6-hydroxy-coumarin prepared in reference example 25 by the same procedure as example 16 (with the proviso that N,N-dimethyl-4-bromobutanamide was used instead of N,N-dimethyl-5-bromopentanamide).
TLC(ethyl acetate) : Rf 0.42;
IR(cm^{-1}) :ν 2935, 1729, 1608, 1505, 1471, 1246, 1219, 1176, 1121, 1038, 969, 847, 803.

Example 17

3-[1-(5E-7-hydroxy-n-pentadecenyl)oxy-4-(4-dimethylaminocarbonylbutyl)oxybenzen-2-yl]propionic acid

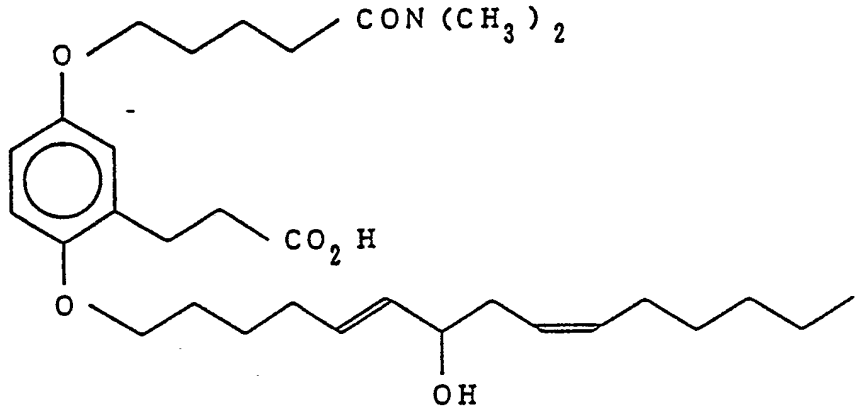


The title compound, of the present invention, having the following physical data was obtained with using 6-hydroxycoumarin prepared in reference example 25 by the same procedure as reference example 26 (with the proviso that N,N-dimethyl-5-bromopentanamide was used instead of ethyl 5-bromopentanoate) → reference example 27 → reference example 2→ reference example 10 → reference example 23 → reference example 14 → reference example 15 → reference example 16 → reference example 5 and then purification by column chromatography on silica gel.
TLC(chloroform : methanol = 10 : 1) : Rf 0.42;
IR(cm^{-1}) :ν 3402, 2928, 2857, 1727, 1626, 1500, 1470, 1402, 1220, 1158, 1058, 972, 804.

Example 17(a) and 17(b)

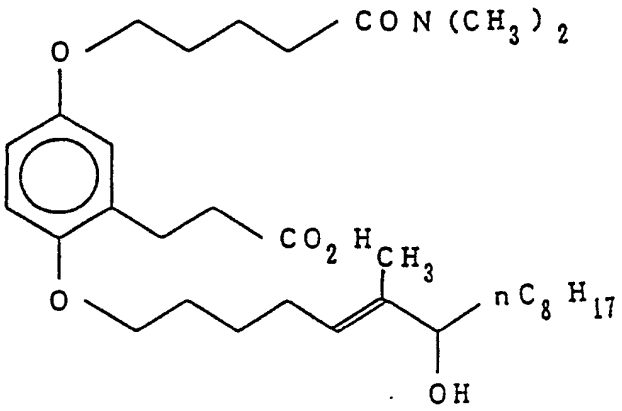
Example 17(a)

3-[1-(5E,9Z-7-hydroxy-n-pentadecadienyl)oxy-4-(4-dimethylaminocarbonylbutyl)oxybenzen-2-yl]propionic acid



Example 17(b)

3-[1-(5E-6-methyl-7-hydroxy-n-pentadecenyl)oxy-4-(4-dimethylaminocarbonylbutyl)oxybenzen-2-yl]propionic acid



The title compound, of the present invention, having the following physical data was obtained with using 6-hydroxy-coumarin, prepared in reference example 25 by the same procedure as example 17 (with the proviso that the corresponding appropriate phosphonate was used instead of dimethyl 2-oxodecyl-phosphonate for the same procedure as reference example 15).

17(a) :

TLC(chloroform : methanol = 10 : 1) : Rf 0.46;

IR(cm^{-1}) : ν 2931, 2860, 1727, 1626, 1500, 1470, 1402, 1220, 1158, 1055, 804.

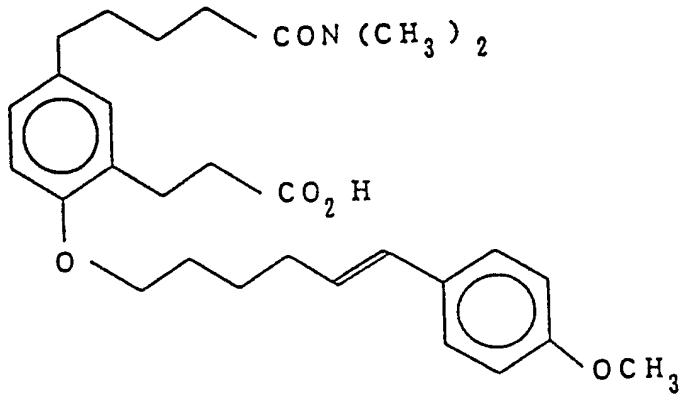
17(b) :

TLC(chloroform : methanol = 10 : 1) : Rf 0.51;

IR(cm^{-1}) :ν 2928, 2857, 1728, 1627, 1500, 1471, 1401, 1220, 1159, 1057, 804.

Example 18

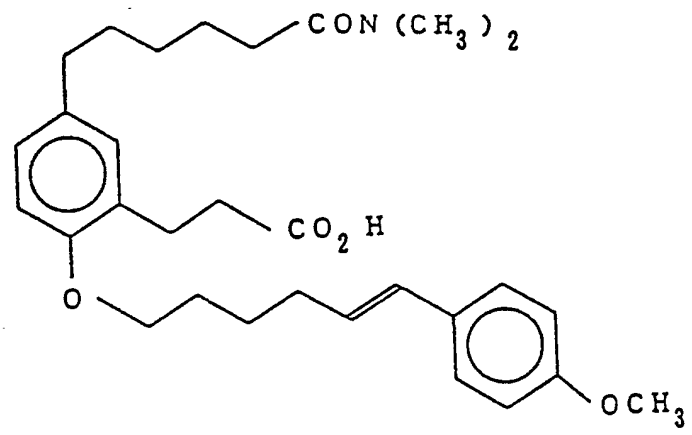
3-[1-[6-(4-methoxyphenyl)hex-5E-enyl]oxy-4-(4-dimethylaminocarbonylbutyl)benzen-2-yl]propionic acid



The title compound, of the present invention, having the following physical data was obtained with using the ester in reference example 31 by the same procedure as reference example 4→ reference example 5 and then purification by column chromatography on silica gel.
TLC(ethyl acetate) : Rf 0.50;
IR(cm^{-1}) : ν 2935, 2861, 1729, 1609, 1510, 1468, 1402, 1249, 1 176, 1121, 1036, 969, 846, 809.

Example 18(a)

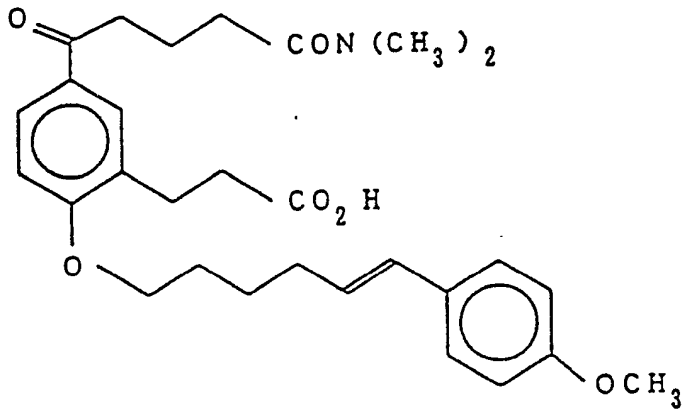
3-[1-[6-(4-methoxyphenyl)hex-5E-enyl]oxy-4-(5-dimethylaminocarbonylpentyl)benzen-2-yl]propionic acid



The title compound, of the present invention, having the following physical data was obtained with using an ester, which was prepared with using 3-(1-methoxybenzen-2-yl)propionic acid by the same procedure as reference example 12 → reference example 28 (with the proviso that methyl 5-(chloroformyl)pentanoate was used instead of methyl 4-(chloroformyl)butyrate) → reference example 16 → reference example 29 → reference example 30 → reference example 31, by the same procedure as example 18.
TLC(ethyl acetate : methanol = 10 : 1) : Rf 0.65;
IR(cm^{-1}) :ν 2933, 2857, 1728, 1609, 1511, 1467, 1402, 1290, 1249, 1176, 1121, 1035, 968, 846, 809, 756.

Example 19

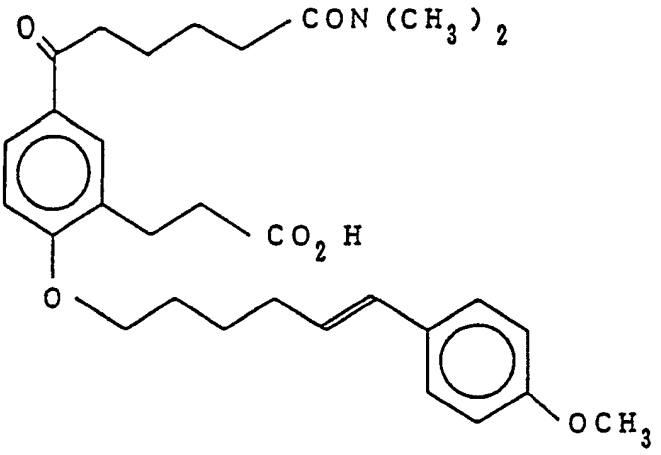
3-[1-[6-(4-methoxyphenyl)hex-5E-enyl]oxy-4-(1-oxo-4-dimethylaminocarbonylbutyl)benzen-2-yl]propionic acid



The title compound, of the present invention, having the following physical data was obtained with using the dicarboxylic acid prepared in reference example 32 by the same procedure as reference example 30 → reference example 27 → reference example 2 → reference example 6 → reference example 4 → reference example 5 and then purification by column chromatography on silica gel.
TLC(ethyl zacetate : methanol = 9 : 1) : Rf 0.56
IR(cm^{-1}) : ν 3448, 2941, 2871, 2519, 1736, 1714, 1674, 1603, 1512, 1470, 1411, 1362, 1334, 1299, 1282, 1254, 1176, 1160, 1126, 1106, 1035.

Example 19(a)

3-[1-[6-(4-methoxyphenyl)hex-5E-enyl]oxy-4-(1-oxo-5-dimethylaminocarbonylpentyl]benzen-2-yl]propionic acid



The title compound, of the present invention, having the following physical data was obtained with using

a dicarboxylic acid, which was prepared with using 3-(1-methoxybenzen-2-yl)propionic acid by the same procedure as reference example 12 → reference example 28 (with the proviso that methyl 5-(chloroformyl)-pentanoate was used instead of methyl 4-(chloroformyl)-butyrate) → reference example 5 → reference example 32, by the same procedure as example 19.

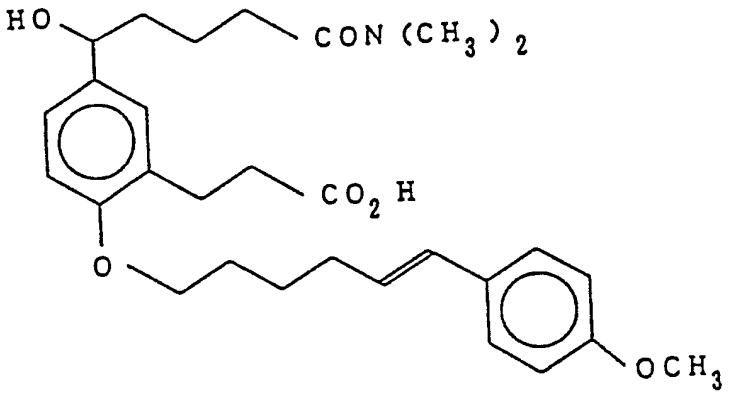
TLC(ethyl acetate : methanol = 10 : 1) : Rf 0.50;

IR(cm^{-1}) : v 3034, 2941, 2872, 1729, 1674, 1617, 1578, 1510, 1466, 1411, 1373, 1315, 1248, 1210, 1176, 1116, 1038, 1016, 998, 972, 845, 817.

Example 20 and 20(a)

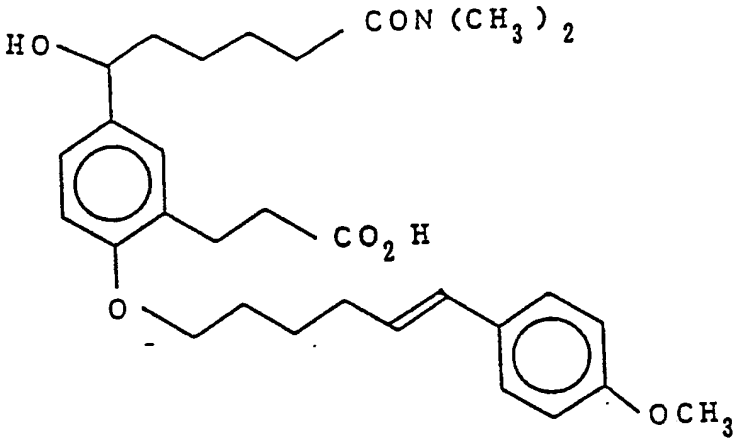
Example 20

3-[1-[6-(4-methoxyphenyl)hex-5E-enyl]oxy-4-(1-hydroxy-4-dimethylaminocarbonylbutyl)benzen-2-yl]-propionic acid



Example 20(a)

3-[1-[6-(4-methoxyphenyl)hex-5E-enyl]oxy-4-(1-hydroxy-5-dimethylaminocarbonylpentyl)benzen-2-yl]-propionic acid



The title compounds, of the present invention, having the following physical data were obtained with using the carboxylic acid prepared in reference example 19 and 19(a) by the same procedure as reference example 16.

Example 20 :

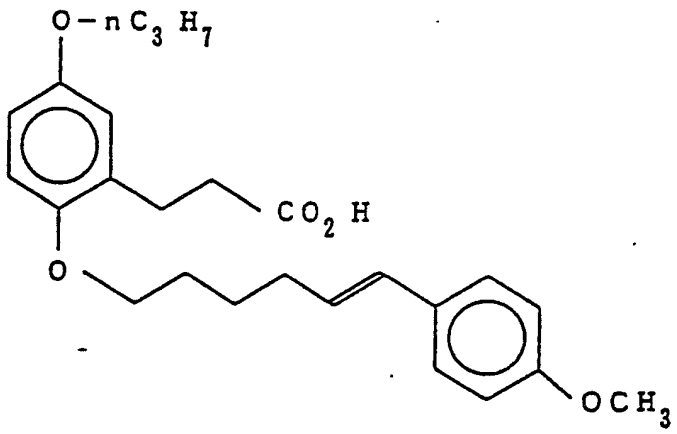
TLC(ethyl acetate : methanol = 9 : 1) : Rf 0.48;
IR(cm^{-1}) : ν 2936, 1723, 1609, 1511, 1468, 1403, 1249, 1176, 1120, 1035,

Example 20(a)

TLC(ethyl acetate : methanol = 10 : 1) : Rf 0.42;
IR(cm^{-1}) ν 2936, 2864, 1725, 1609, 1511, 1467, 1403, 1249, 1176, 1119, 1035, 969, 814, 756.

Example 21

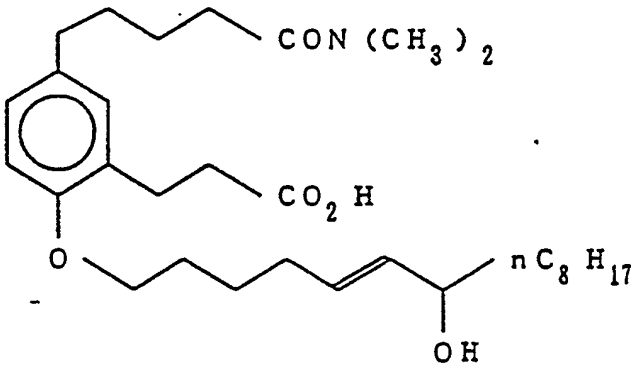
3-[1-[6-(4-methoxyphenyl)hex-5E-enyl]oxy-4-n-propoxybenzen-2-yl]propionic acid



The title compound, of the present invention, having the following physical data was obtained with using 6-hydroxy-coumarin prepared in reference example 25 by the same procedure as reference example 26 (with the proviso that 1-bromo-n-propane was used instead of ethyl 5-bromopentanoate) → reference example 27 → reference example 2 → reference example 4 → reference example 5 and then purification by column chromatography on silica gel.
TLC(ethyl acetate : n-hexane = 1 : 1) : Rf 0.30;
IR(cm^{-1}) : ν 2937, 1713, 1608, 1504, 1471, 1217, 1036.

Example 22

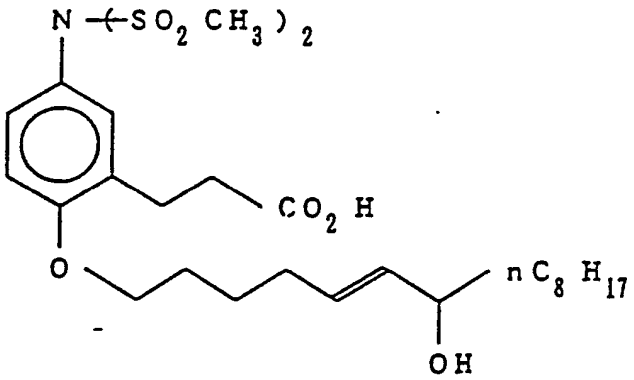
3-[1-(5E-7-hydroxy-n-pentadecenyl)oxy-4-(4-dimethylaminocarbonyl-n-butyl)benzen-2-yl]propionic acid



The title compound, of the present invention, having the following physical data was obtained with using the ethyl ester prepared in reference example 31 by the same procedure as reference example 10 → reference example 23 → reference example 14 → reference example 15 →reference example 16 → reference example 5 and then purification by column chromatography on silica gel.
TLC(ethyl acetate) : Rf 0.42;
IR(cm^{-1}) : ν 3402, 2927, 2856, 1728, 1626, 1504, 1468, 1402, 1251, 1161, 1121, 1058, 971, 908, 810, 723.

Example 23

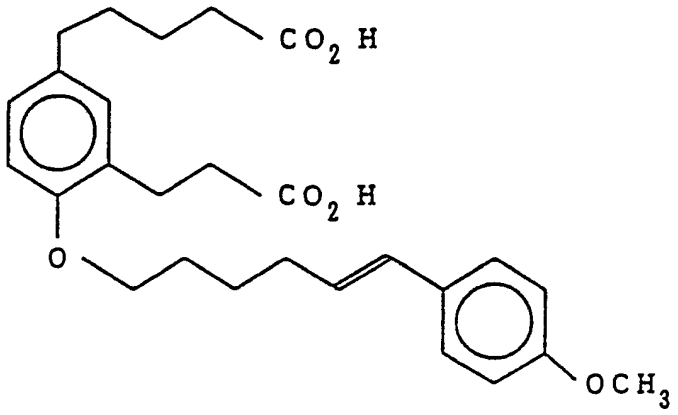
3-[1-(5E-7-hydroxy-n-pentadecenyl)oxy-4-dimesylaminobenzen-2-yl]propionic acid



The title compound, of the present invention, having the following physical data was obtained with using the tert-butyl ester prepared in reference example 17 by the same procedure as reference example 10 → reference example 18 → reference example 20 → reference example 11 → reference example 12 → reference example 13 → reference example 14 → reference example 15 → reference example 16 → reference example 5 and then purification by column chromatography on silica gel.
TLC(ethyl acetate) : Rf 0.40;
IR(cm^{-1}) :ν 3368, 2921, 2856, 1714, 1504, 1373, 1325, 1261, 1219, 1158, 976, 921, 871, 762.

Example 24

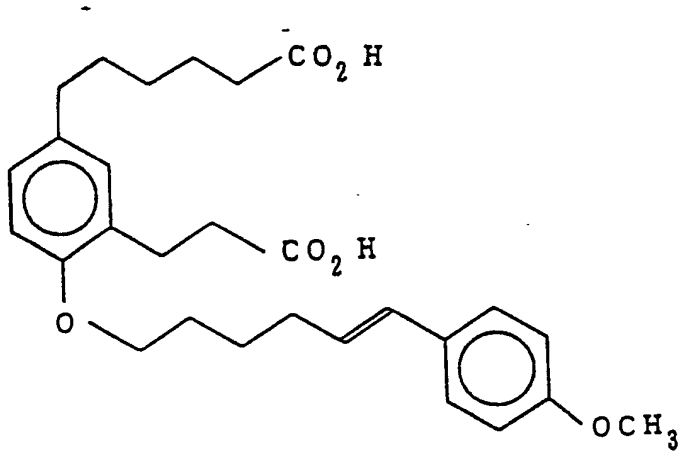
3-[1-[6-(4-methoxyphenyl)hex-5E-enyl]oxy-4-(4-carboxylbutyl)benzen-2-yl]propionic acid



The title compound, of the present invention, having the following physical data was obtained with using the dicarboxylic acid prepared in reference example 29 by the same procedure as reference example 31 → reference example 4 → reference example 5 and then purification by column chromtography on silica gel.
TLC(ethyl acetate : methanol = 6 : 1) : Rf 0.70;
IR(cm^{-1}) : ν 3015, 2938, 2857, 1702, 1610, 1514, 1503, 1473, 1463, 1447, 1422, 1408, 1341, 1305, 1288, 1250, 1202, 1179, 1118, 1040, 1020, 963, 807

Example 24(a)

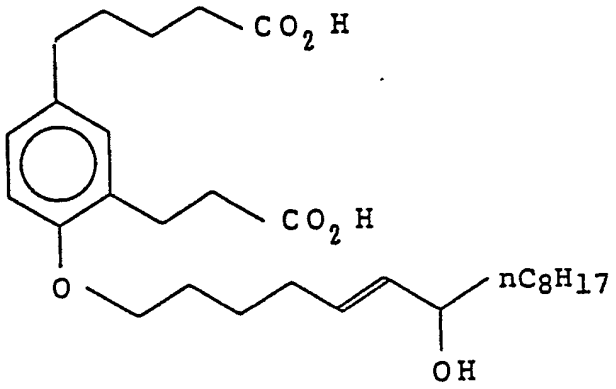
3-[1-[6-(4-methoxyphenyl)hex-5E-enyl]oxy-4-(5-carboxylpentyl)benzen-2-yl]propionic acid



The title compound, of the present invention, having the following physical data was obtained with using a dicarboxylic acid, which was prepared with using 3-(1-methoxybenzen-2-yl)propionic acid by the same procedure as reference example 12 → reference example 28 (with the proviso that methyl 5-(chloroformyl)-pentanoate was used instead of methyl 4-(chloroformylbutyrate) → reference example 29, by the same procedure as example 24.
TLC(ethyl acetate : methanol = 20 : 1) : Rf 0.68;
IR(cm^{-1}) : ν 2932, 2853, 1709, 1609, 1512, 1500, 1465, 1420, 1289, 1245, 1206, 1176, 1128, 1031, 966, 836, 814, 800.

Example 25

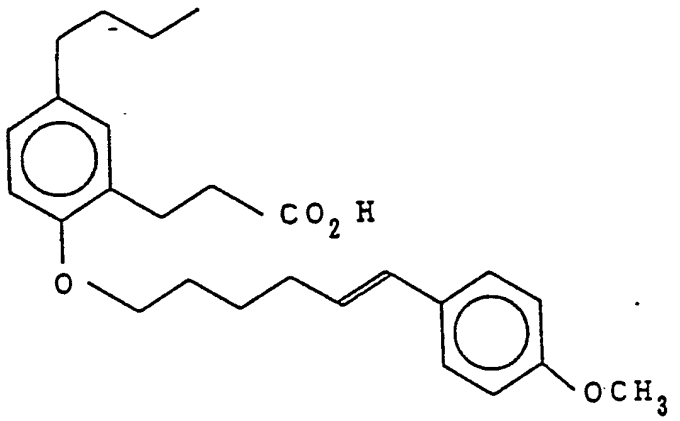
3-[1-(5E-7-hydroxy-n-pentadecenyl)oxy-4-(4-carboxyl-n-butyl)benzen-2-yl]propionic acid



The title compound, of the present invention, having the following physical data was obtained with using the carboxylic acid prepared in reference example 29 by the same procedure as reference example 31 → reference example 10 → reference example 23 → reference example 14 → reference example 15 → reference example 16 → reference example 5 and then purification by column chromatography on silica gel.
TLC(ethyl acetate) : Rf 0.33;
IR(cm^{-1}) : ν 3426, 2922, 2855, 1719, 1703, 1611, 1503, 1465, 1447, 1429, 1409, 1311, 1286, 1241, 1199, 1127, 1059, 1001, 975, 960, 806.

Example 26

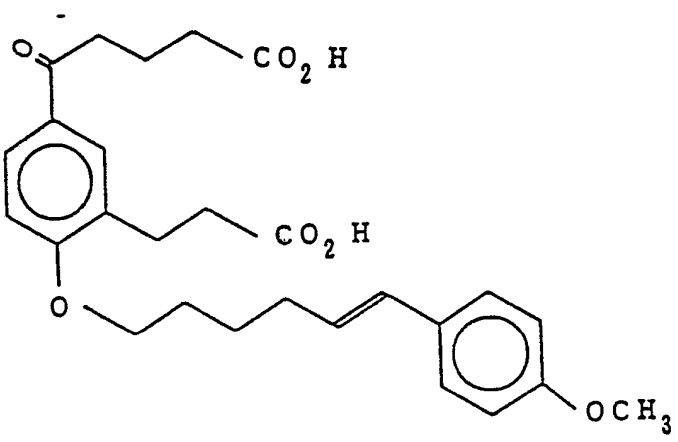
3-[1-[6-(4-methoxyphenyl)hex-5E-enyl]oxy-4-n-butylbenzen-2-yl]propionic acid



The title compound, of the present invention, having the following physical data was obtained with using 3-(1-methoxybenzen-2-yl)propionic acid by the same procedure as reference example 12 → reference example 28 (with the proviso that butyryl chloride was used instead of methyl 4-(chloroformyl)-butyrate) → reference example 16 → reference example 29 → reference example 31 → reference example 4 → reference example 5 and then purification by column chromatography on silica gel.
TLC(n-hexane : ethyl acetate = 2 : 1) : Rf 0.48;
IR(cm^{-1}) : ν 3003, 2931, 2858, 1708, 1609, 1577, 1510, 1467, 1456, 1442, 1290, 1247, 1224, 1175, 1124, 1037, 967, 844, 804.

Example 27

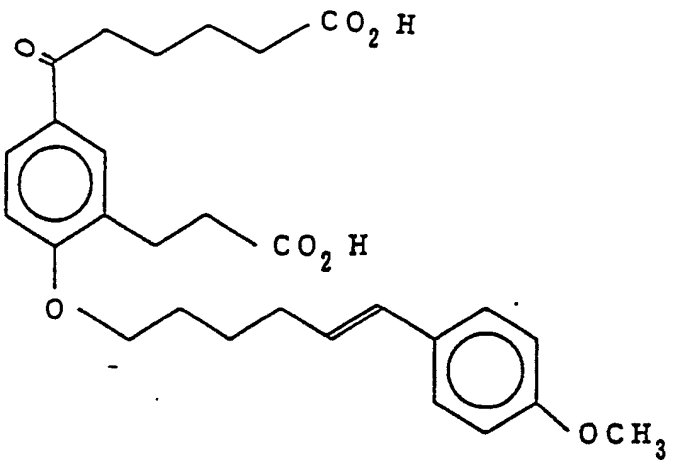
3-[1-[6-(4-methoxyphenyl)hex-5E-enyl]oxy-4(1-oxo-4-carboxylbutyl)benzen-2-yl]propionic acid



The title compound, of the present invention, having the following physical data was obtained with using the dicarboxylic acid prepared in reference example 32 by the same procedure as reference example 31 → reference example 4 → reference example 5 and then purification by column chlomatography on silica gel.
TLC(ethyl acetate : methanol = 9 : 1) : Rf 0.20;
IR(cm^{-1}) : ν 2943, 1697, 1682, 1603, 1510, 1259, 1117

Example 27(a)

3-[1-[6-(4-methoxyphenyl)hex-5E-enyl]oxy-4-(1-oxo-5-carboxylpentyl)benzen-2-yl]propionic acid

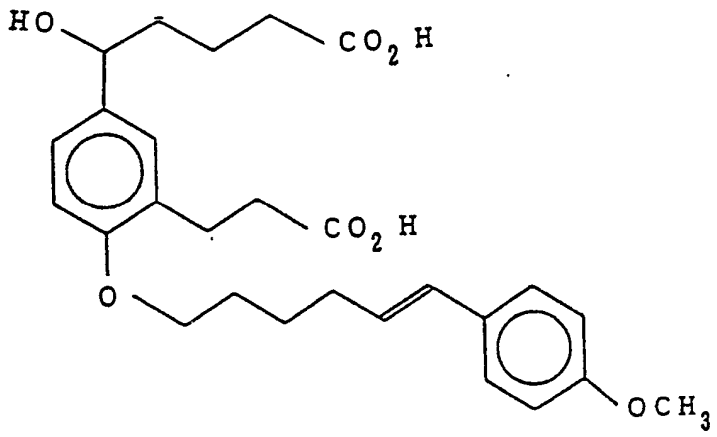


The title compound, of the present invention, having the following physical data was -obtained with using a dicarboxylic acid, which was prepared with using 3-(1-methoxybenzen-2-yl)propionic acid by the same procedure as reference example 12 → reference example 28 (with the proviso that methyl 4-(chloroformyl)pentanoate was used instead of methyl 4-(chloroformyl)butyrate) → reference example 5 → reference example 32, by the same procedure as example 27.

TLC(ethyl acetate : methanol = 20 : 1) : Rf 0.45;
IR(cm^{-1}) :ν 2939, 1709, 1694, 1682, 1604, 1578, 1511, 1300, 1260, 1245, 1179, 1116, 1037, 973.

Example 28

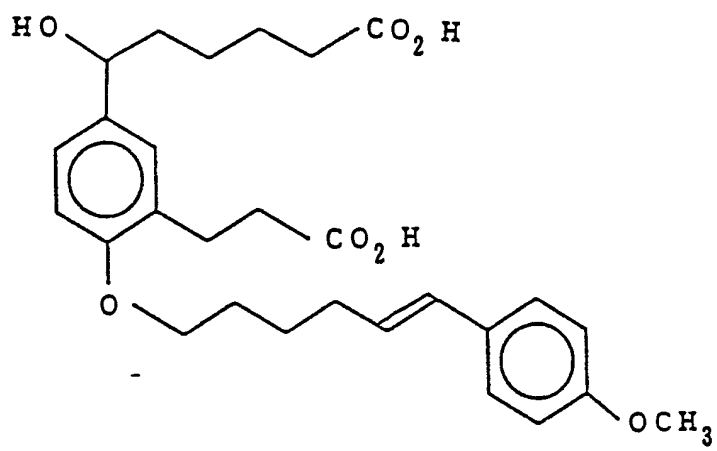
3-[1-[6-(4-methoxyphenyl)hex-5E-enyl]oxy4-(1-hydroxy-4-carboxylbutyl)benzen-2-yl]propionic acid



The title compound, of the present invention, having the following physical data was obtained with using the dicarboxylic acid prepared in example 27 by the same procedure as reference example 16.
TLC(ethyl acetate : methanol = 9 : 1) : Rf 0.20;
IR(cm^{-1}) :ν 3401, 2938, 1608, 1558, 1511, 1409, 1249, 1176, 1119, 1034, 968, 810.

Example 28(a)

3-[1-[6-(4-methoxyphenyl)hex-5E-enyl]oxy-4-(1-hydroxy-5-carboxylpentyl)benzen-2-yl]propionic acid

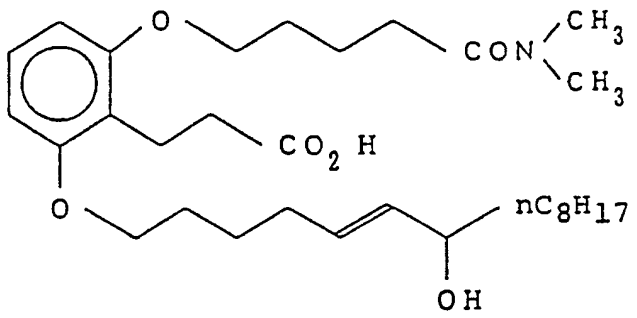


The title compound, of the present invention, having the following physical data was obtained with using the dicarboxylic acid prepared in example 27(a) by the same procedure as example 28.

TLC(ethyl acetate : methanol = 20 : 1) : Rf 0.47;
IR(cm^{-1}) : ν 3555, 3032, 2932, 2861, 1703, 1609, 1513, 1503, 1467, 1449, 1427, 1408, 1286, 1250, 1211, 1178, 1122, 1036, 963, 808.

Example 29

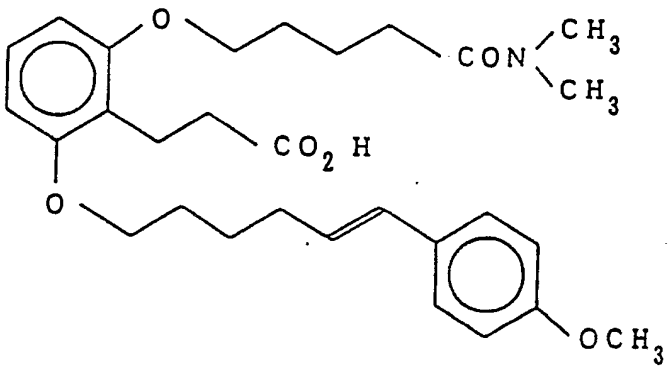
3-[1-(5E-7-hydroxypentadecenyl)oxy-3-(4-dimethylaminocarbonylbutyl)oxybenzen-2-yl]propionic acid



A residue was obtained with using 2,6-dimethoxybenzaldehyde by the same procedure as reference example 24 → reference example 2 → reference example 25 → reference example 26 (with the proviso that N,N-dimethyl-5-bromopentanamide was used instead of ethyl 5-bromopentanoate) → reference example 27 → reference example 10 → reference example 23 → reference example 14 → reference example 15 → reference example 16 → reference example 5. The residue was purified by column chromatography on silica gel (chloroform : methanol = 20 : 1) to give the title compound having the following physical data.
TLC(chloroform : methanol = 10 : 1) : Rf 0.44;
IR(cm^{-1}) : ν 2927, 2856, 1723, 1596, 1463, 1402, 1255, 1183, 1161, 1103, 971, 776, 725

Example 30

3-[1-[6-(4-methoxyphenyl)hex-5E-enyl]oxy-3-(4-dimethylaminocarbonylbutyl)oxybenzen-2-yl]propionic acid

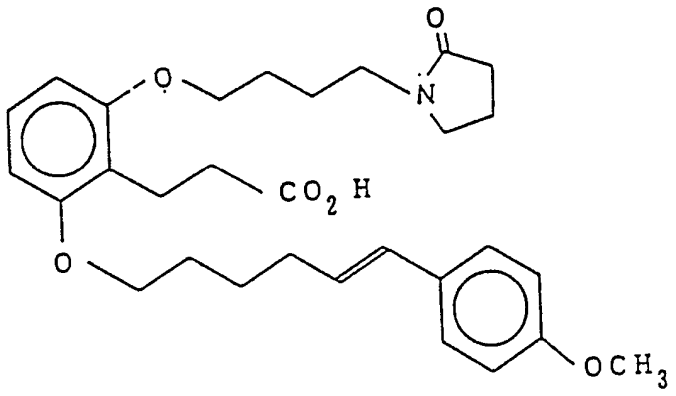


The title compound, of the present invention, having the following physical data was obtained with using 2,6-dimethoxybenzaldehyde by the same procedure as reference example 24 → reference example 2 → reference example 25 → reference example 26 (with the proviso that N,N-dimethyl-5-bromopentanamide was used instead of ethyl 5-bromopentanoate) → reference example 27 → reference example 4 → reference

example 5 and then purification by column chromatography on silica gel.
TLC(chloroform : methanol = 10 : 1) : Rf 0.52;
IR(cm^{-1}) :ν 2937, 1723, 1608, 1596, 1511, 1463, 1401, 1250, 1178, 1103, 1035, 969, 846, 776, 756.

Example 30(a)

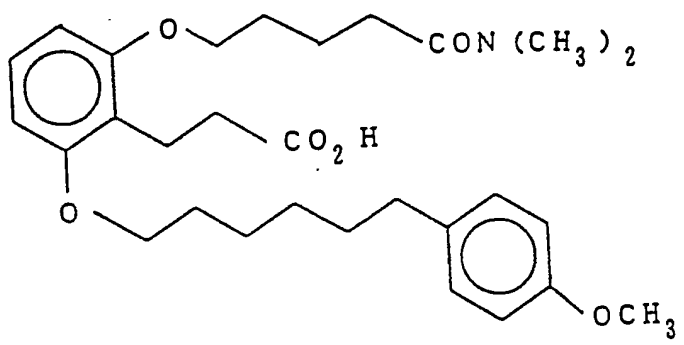
3-[1-[6-(4-methoxyphenyl)hex-5E-enyl]oxy-3[4-(2-pyrrolidon-1-yl)-n-butoxy]benzen-2-yl]propionic acid



The title compound, of the present invention, having the following physical data was obtained with using 2,6-dimethoxybenzaldehyde by the same procedure as example 30 (with the proviso that 1-bromo-4-(2-pyrrolidon-1-yl)butane was used instead of N,N-dimethyl-5-bromopentanamide)
TLC(chloroform : methanol = 10 : 1) : Rf 0.45;
IR(cm^{-1}) : ν 2937, 1723, 1645, 1595, 1511, 1463, 1389, 1250, 1178, 1103, 1035, 969, 847, 756.

Example 30(b)

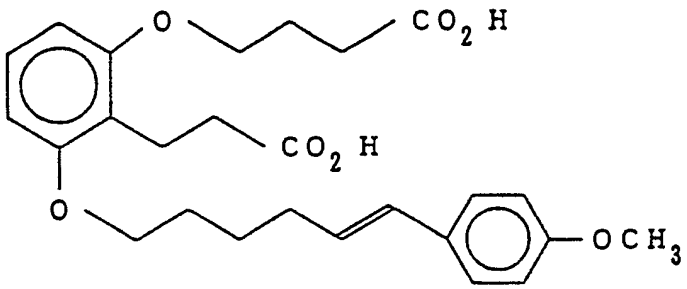
3-[1-[6-(4-methoxyphenyl)hexyl]oxy-3-(4-dimethylaminocarbonylbutyl)oxybenzen-2-yl]propionic acid



the title compound, of the present invention, having the following physical data was obtained with using 2,6-dimethoxybenzaldehyde by the same procedure as example 30 (with the proviso that 6-(p-methoxyphenyl)hexanol methansulfonate was used instead of 6-(p-methoxyphenyl)-5E-hexenol methansulfonate).
TLC(ethylacetate : methanol = 9 : 1) : Rf 0.30;
IR(cm^{-1}) :ν 2933, 1724, 1596, 1513, 1463, 1248, 1103.

Example 31

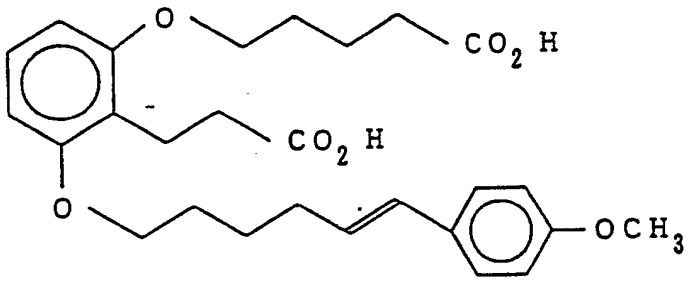
3-[1-[6-(4-methoxyphenyl)hex-5E-enyl]oxy-3-(3-carboxylpropyl)oxybenzen-2-yl]propionic acid



The title compound, of the present invention, having the following physical data was obtained with using 2,6-dimethoxybenzaldehyde by the same procedure as reference example 24 → reference example 2 → reference example 25 → reference example 26 (with the proviso that ethyl 4-bromobutyrate was used instead of ethyl 5-bromopentanoate) → reference example 27 → reference example 4 → reference example 5 and purification by column chromatography on silica gel.
TLC(chloroform : methanol = 10 : 1) : Rf 0.35;
IR(cm^{-1}) : ν 2937, 1707, 1559, 1511, 1463, 1250, 1177, 1104, 1036, 967, 846, 775, 729.

Example 31(a)

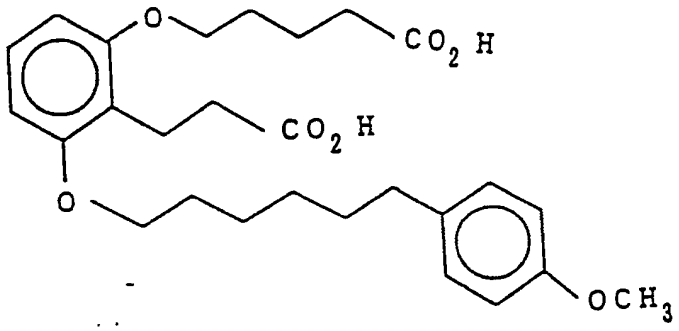
3-[1-[6-(4-methoxyphenyl)hex-5E-enyl]oxy-3-(4-carboxylbutyl)oxybenzen-2-yl]propionic acid



The title compound, of the present invention, having the following physical data was obtained with using 2,6-dimethoxybenzaldehyde by the same procedure as example 31 (with the proviso that ethyl 5-bromopentanoate was used instead of ethyl 4-bromobutyrate).
TLC(chloroform : methanol = 10 : 1) : Rf 0.37;
IR(cm^{-1}) :ν 2937, 1699, 1595, 1510, 1460, 1250, 1180, 1160, 1034, 967, 846, 773, 718

Example 31(b)

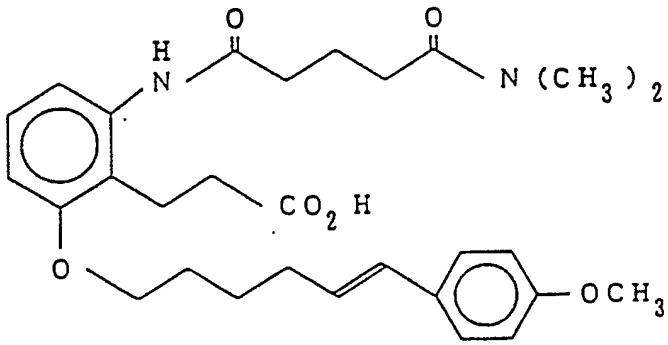
3-[1-[6-(4-methoxyphenyl)hexyl]oxy-3-(4-carboxylbutyl)oxybenzen-2-yl]propionic acid



The title compound, of the present invention, having the following physical data was obtained with using the compound prepared in example 31(a) by the same procedure as reference example 2 and then purification by column chromatography on silica gel.
TLC(ethyl acetate : methanol = 9 : 1) : Rf 0.40;
IR(cm^{-1}) : ν 2935, 1702, 1595, 1513, 1461, 1245, 1104.

Example 32

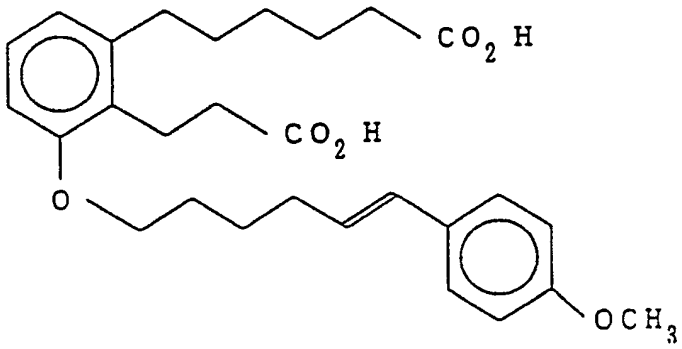
3-[1-[6-(4-methoxyphenyl)hex-5E-enyl]oxy-3-(4-dimethylaminocarbonylbutanamido)benzen-2-yl]propionic acid



The title compound, of the present invention, having the following physical data was obtained with using 2-hydroxy-6-nitrobenzaldehyde, which was prepared with using 3-nitrophenol by the method described in Bull. Chem. Soc. Japan, 46. 2903 (1973), by the same procedure as reference example 1 → reference example 2 → reference example 3 → reference example 4 → reference example 5 → refernce example 6 (with the proviso that dimethylamine was used instead of morpholine) → example 1.
TLC(methylene chloride : methanol = 4 : 1) : Rf 0.52;
IR(cm^{-1}) : ν 2936, 1608, 1511, 1456, 1248, 1176.

Example 33

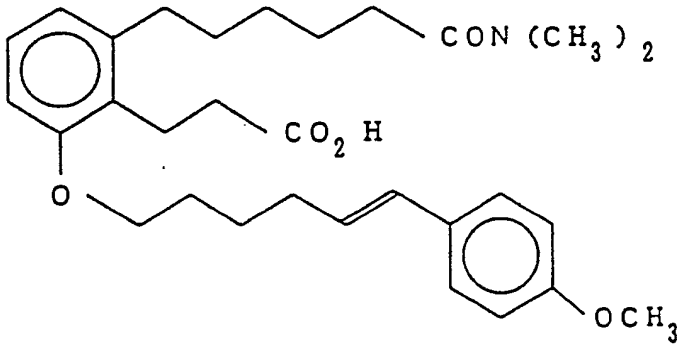
3-[1-[6-(4-methoxyphenyl)hex-5E-enyl]oxy-3-(5-carboxylpentyl)benzen-2-yl]propionic acid



The title compound, of the present invention, having the following physical data was obtained with using an ester, which was prepared with using the ester prepared in reference example 36 by the same procedure as reference example 4, by the same procedure as reference example 5 and then pruification by column chromatography on silica gel.
TLC(chloroform : methanol = 10 : 1) ; Rf 0.30;
MS : m/z 468(M^+), 189;
IR(cm^{-1}) : ν 2930, 1707, 1608, 1583, 1511, 1458, 1248, 1176, 1088, 1037, 967, 846, 756.

Example 34

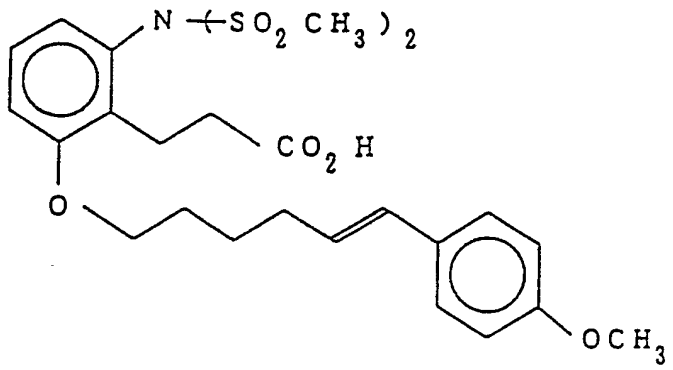
3-[1-[6-(4-methoxyphenyl)hex-5E-enyl]oxy-3-(5-dimethylaminocarbonylpentyl)benzen-2-yl]propionic acid



The title compound, of the present invention, having the following physical data was obtained with using the ester prepared in reference example 36 by the same procedure as reference example 25 → reference example 6 (with the proviso that dimethylamine was used instead of morpholine) → reference example 27 → reference example 4 → reference example 5 and then purification by column chromatography on silica gel.
TLC(chloroform : methanol = 10 : 1) : Rf 0.48;
IR(cm^{-1}) : ν 2932, 1724, 1609, 1510, 1458, 1402, 1249, 1176, 1087, 1037, 969, 847, 791, 751.

Example 35

3-[1-[6-(4-methoxyphenyl)hex-5E-enyl]oxy-3-dimesylaminobenzen-2-yl]propionic acid

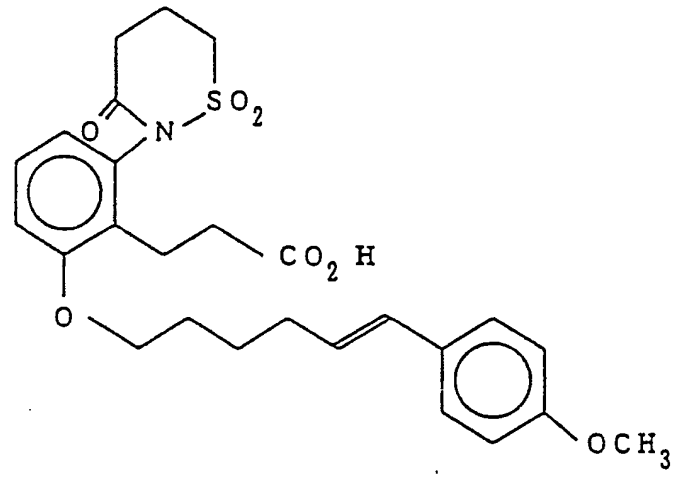


The title compound, of the present invention, having the following physical data was obtained with using 2-hydroxy-6-nitrobenzaldhyde by the same procedure as reference example 1 → reference example 2 → reference example 17 → reference example 4 → reference example 18 → reference example 20 → example 1.

NMR : δ 1.67 (2H, m), 1.88 (2H, m), 2.27 (2H, m), 2.73 (2H, m), 3.09 (2H, m), 3.47 (6H, s), 3.80 (3H, s), 4.03 (2H, t), 6.08 (1H, dt), 6.35 (1H, d), 6.79-7.02 (4H, m), 7.18-7.33 (3H, m).

Example 36

3-[1-[6-(4-methoxyphenyl)hex-5E-enyl]oxy-3-(perhydro-1,2-thiazin-1,1,3-trione-2-yl)benzen-2-yl]propionic acid

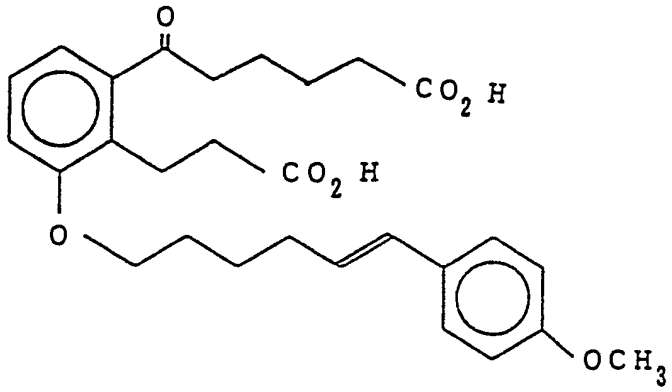


The title compound, of the present invention, having the following physical data was obtained with using 2-hydroxy-6-nitrobenzaldehyde by the same procedure as reference example 1 → reference example 2 → reference example 17 → reference example 4 → reference example 18 → reference example 3 → reference example 5 → reference example 22 → example 1.

NMR : δ 166 (2H, m), 1.86 (2H, m), 2.27 (2H, m), 2.44 (2H, m), 2.63 (2H, m), 2.77-3.00 (4H, m), 3.59 (2H, t, J = 6Hz), 3.79 (3H, s), 4.02 (2H, m), 6.08 (1H, dt, J = 16Hz, 7Hz), 6.35 (1H, d, J = 16Hz), 6.78-6.99 (4H, m), 7.l8-7.34 (3H, m).

Example 37

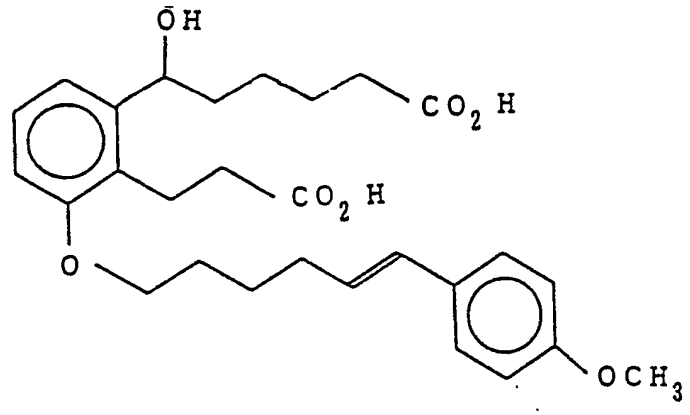
3-[1-[6-(4-methoxyphenyl)hex-5E-enyl]oxy-3-(1-oxo-5-carboxylpentyl)pentyl)benzen-2-yl]propionic acid



A residude was obtained with using the carboxylic acid prepared in reference example 40 by the same proceure as reference examples 25 → reference example 27 → reference example 31 → reference example 4 → reference example 5. The residue was purified by column chromatography on silica gel (chloroform : methanol = 20 : 1 → 10 : 1) to give the title compound, of the present invention, having the following physical data. TLC(chloroform : methanol + 10 : 1) : Rf 0.32;
IR(cm^{-1}) : ν 2934, 1706, 1608, 1579, 1511, 1454, 1248, 1176, 1036, 968, 846, 757.

Example 38

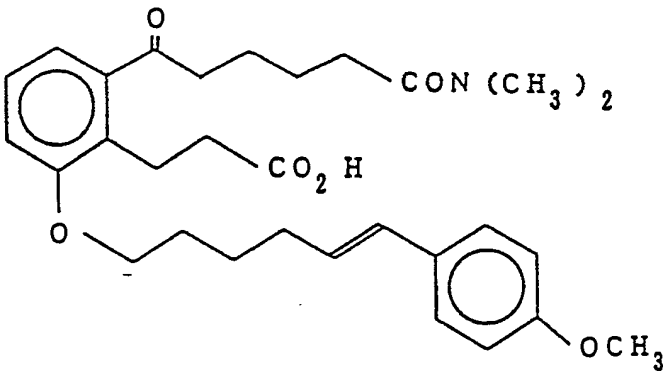
3-[1-[6-(4-methoxyphenyl)hex-5E-enyl]oxy-3-(1-hydroxy-5-carboxylpentyl)benzen-2-yl]propionic acid



The title compound, of the present invention, having the following physical data was obtained with using the carboxylic acid prepared in example 37 by the same procedure as reference example 16.
TLC(chloroform : methanol = 10 : 1) : Rf 0.24;
IR(cm^{-1}) : ν 2937, 1708, 1608, 1585, 1511, 1459, 1250, 1176, 1036, 968, 846, 794, 756.

Example 39

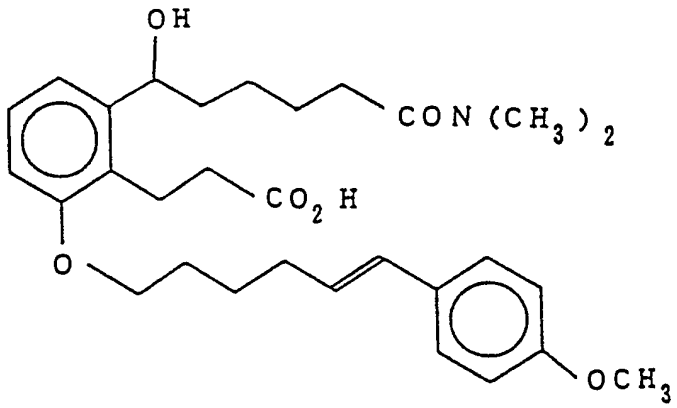
3-[1-[6-(4-methoxyphenyl)hex-5E-enyl]oxy-3-(1-oxo-5-dimethylaminocarbonylpentyl)benzen-2-yl]propionic acid



The title compound, of the present invention, having the following physical data was obtained with using the carboxylic acid prepared in reference example 40 by the same procedure as reference example 25 → reference example 27 → reference example 6 (with the proviso that dimethylamine was used instead of morpholine) → reference example 4 → reference example 5 and then purification by column chromatography on silica gel.
TLC(chloroform : methanol = 10 : 1) : Rf 0.48;
IR(cm^{-1}) : ν 2942, 1723, 1674, 1626, 1577, 1512, 1453, 1418, 1398, 1250, 1181, 1018, 987, 964, 907, 842, 812, 785, 744.

Example 40

3-[1-[6-(4-methoxyphenyl)hex-5E-enyl]oxy-3-(1-hydroxy-5-dimethylaminocarbonylpentyl)benzen-2-yl]-propionic acid



The title compound, of the present invention, having the following physical data was obtained with using the carboxylic acid prepared in example 39 by the same procedure as reference example 16.
TLC(chloroform : methanol = 10 : 1) : Rf 0.35;
IR(cm^{-1}) : ν 2937, 1718, 1608, 1511, 1460, 1403, 1249, 1176, 1067, 1036, 969, 847, 795, 755.

Formulation Example 1

The following components were admixed in conventional method and punched out to obtain 100 tablets

each containing 50 mg of active ingredient.

- 3-[1-[6-(4-methoxyphenyl)hex-5E-enyl]oxy-3-(4-carboxylbutyl)oxybenzen-2-yl]propionic acid ----- 5.0 g
- Cellulose calcium glycolate (carboxymethylcellulose calcium) (disintegrating agent) ----- 0.2 g
- Magnesium stearate (Lubricating agent) ----- 0.1 g
- Microcrystaline cellulose ----- 4.7 g

Names of the compounds in the tables

Ex. No.	Name
1(a)	3-[1-[6-(4-methoxyphenyl)hex-5E-enyl]oxy-4-(4-dimethylaminocarbonylbutanamido)benzen-2-yl]propionic acid
1(b)	3-[1-n-hexyloxy-4-(4-dimethylaminocarbonyl-butanamido)benzen-2-yl]propionic acid
1(c)	3-[1-n-dodecyloxy-4-(4-dimethylaminocarbonyl-butanamido)benzen-2-yl]propionic acid
1(d)	3-[1-n-hexadecyloxy-4-(4-dimethylaminocarbonyl-butanamido)benzen-2-yl]propionic acid
1(e)	3-[1-[6-(4-n-propoxyphenyl)hex-5E-enyl]oxy-4-(4-dimethylaminocarbonylbutanamido)benzen-2-yl]propionic acid
1(f)	3-[1-[6-[4-(2-propenyl)oxyphenyl]hex-5E-enyl]oxy-4-(4-dimethylaminocarbonylbutanamido)benzen-2-yl]propionic acid
1(g)	3-[1-[7-(4-methoxyphenyl)hept-6E-enyl]oxy-4-(4-dimethylaminocarbonylbutanamido)benzen-2-yl]propionic acid
1(h)	3-[1-[7-(4-methoxyphenyl)-n-heptyl]oxy-4-(4-dimethylaminocarbonylbutanamido)benzen-2-yl]propionic acid
1(i)	3-[1-[6-(4-n-pentyloxyphenyl)hex-5E-enyl]oxy-4-(4-dimethylaminocarbonylbutanamido)benzen-2-yl]propionic acid

Ex. No.	Name
1(j)	3-[1-[6-(4-methoxyphenyl)-n-hexyl]oxy-4-(4-dimethylaminocarbonylbutanamido)benzen-2-yl]propionic acid
1(k)	3-[1-(7-phenylhept-6E-enyl)oxy-4-(4-dimethylaminocarbonylbutanamido)benzen-2-yl]propionic acid
1(l)	3-[1-[6-(2-methoxyphenyl)hex-5E-enyl]oxy-4-(4-dimethylaminocarbonylbutanamido)benzen-2-yl]propionic acid
1(m)	3-[1-[6-(3-methoxyphenyl)hex-5E-enyl]oxy-4-(4-dimethylaminocarbonylbutanamido)benzen-2-yl]propionic acid
1(n)	3-[1-[6-(4-methoxyphenyl)hex-5E-enyl]oxy-4-[4-(1-indolinyl)carbonylbutanamido]benzen-2-yl]propionic acid
1(o)	3-[1-[6-(4-methoxyphenyl)hex-5E-enyl]oxy-4-[4-(2-thiazolyl)aminocarbonylbutanamido]benzen-2-yl]propionic acid
1(p)	3-[1-[6-(4-methoxyphenyl)hex-5E-enyl]oxy-4-(3-dimethylaminocarbonylpropionamido)benzen-2-yl]propionic acid
1(q)	3-[1-[6-(4-methylthiophenyl)hex-5E-enyl]oxy-4-(4-dimethylaminocarbonylbutanamido)benzen-2-yl]propionic acid
1(r)	3-[1-[6-(3,4-dimethoxyphenyl)hex-5E-enyl]oxy-4-(4-dimethylaminocarbonylbutanamido)benzen-2-yl]propionic acid

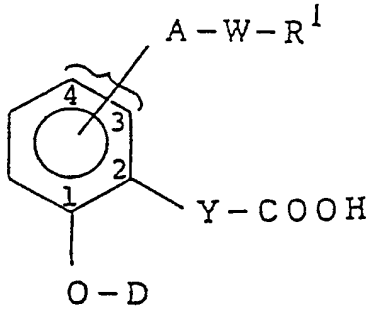
Ex. No.	Name
1(s)	3-[1-[6-(4-methylphenyl)hex-5E-enyl]oxy-4-(4-dimethylaminocarbonylbutanamido)benzen-2-yl]propionic acid
1(t)	3-[1-[6-(4-chlorophenyl)hex-5E-enyl]oxy-4-(4-dimethylaminocarbonylbutanamido)benzen-2-yl]propionic acid
1(u)	3-[1-[6-(4-methoxyphenyl)hex-5E-enyl]oxy-4-(3-dimethylaminocarbonylbenzamido)benzen-2-yl]propionic acid
2(a)	3-[1-[6-(4-methoxyphenyl)hex-5E-enyl]oxy-4-(4-carboxylbutanamido)benzen-2-yl]-E-acrylic acid
2(b)	3-[1-[6-(4-methoxyphenyl)hex-5E-enyl]oxy-4-(3-carboxylbenzamido)benzen-2-yl]propionic acid
3(a)	3-[1-[6-(4-methoxyphenyl)hex-5E-enyl]oxy-4-benzamidobenzen-2-yl]propionic acid
3(b)	3-[1-[6-(4-methoxyphenyl)hex-5E-enyl]oxy-4-decanamidobenzen-2-yl]propionic acid
3(c)	3-[1-[6-(4-methoxyphenyl)hex-5E-enyl]oxy-4-acetamidobenzen-2-yl]propionic acid
4(a)	3-[1-[6-(4-methoxyphenyl)hex-5E-enyl]oxy-4-(4-hydroxybutanamido)benzen-2-yl]propionic acid
4(b)	3-[1-[6-(4-methoxyphenyl)hex-5E-enyl]oxy-4-(3-hydroxymethylbenzamido)benzen-2yl]propionic acid

Ex. No.	Name
5(a)	3-[1-(4E-6-hydroxytetradecenyl)oxy-4-dimethylamino-carbonylbutanamidobenzen-2-yl]propionic acid
5(b)	3-[1-(5E-7-hydroxydodecenyl)oxy-4-dimethylamino-carbonylbutanamidobenzen-2-yl]propionic acid
5(c)	3-[1-[5E-7-hydroxy-9-(4-methoxyphenyl)nonenyl]oxy-4-dimethylaminocarbonylbutanamidobenzen-2-yl]propionic acid
5(d)	3-[1-(5E-7-hydroxynonenyl)oxy-4-dimethylamino-carbonylbutanamidobenzen-2-yl]propionic acid
5(e)	3-[1-(5E-7-hydroxy-7-cyclohexylheptenyl)oxy-4-dimethylaminocarbonylbutanamidobenzen-2-yl]propionic acid
6(a)	3-[1-[6-(4-methoxyphenyl)hex-5E-enyl]oxy-4-(4-methylphenyl)sulfonylaminobenzen-2-yl]propionic acid
6(b)	3-[1-[6-(4-methoxyphenyl)hex-5E-enyl]oxy-4-methyl-sulfonylaminobenzen-2-yl]propionic acid
6(c)	3-[1-[6-(4-methoxyphenyl)hex-5E-enyl]oxy-4-benzyl-sulfonylaminobenzen-2-yl]propionic acid
10(a)	3-[1-[6-(4-methoxyphenyl)hex-5E-enyl]oxy-4-ditosylaminobenzen-2-yl]propionic acid
10(b)	3-[1-[6-(4-methoxyphenyl)hex-5E-enyl]oxy-4-bis(n-butylsulfonyl)aminobenzen-2-yl]propionic acid
10(c)	3-[1-[6-(4-methoxyphenyl)hex-5E-enyl]oxy-4-bis(benzylsulfonyl)aminobenzen-2-yl]propionic acid

Ex. No.	Name
12(a)	3-[1-[6-(4-methoxyphenyl)hexyl]oxy-4-(perhydro-1,2-thiazin-1,1,3-trione-2-yl)benzen-2-yl]propionic acid
12(b)	3-[1-[6-(4-methoxyphenyl)hex-5E-enyl]oxy-4-(isothiazolidin-1,1,3-trione-2-yl)benzen-2-yl]propionic acid
15(a)	3-[1-[5E-7-hydroxy-9-(4-methoxyphenyl)nonenyl]oxy-4-(4-carboxylbutyl)oxybenzen-2-yl]propionic acid
15(b)	3-[1-(5E-7-hydroxypentadecenyl)oxy-4-(3-carboxylpropyl)oxybenzen-2-yl]propionic acid
15(c)	3-[1-(5E-7-hydroxypentadecenyl)oxy-4-carboxylmethoxybenzen-2-yl]propionic acid

Claims

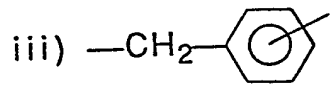
1) A phenylkan(en)oic acid of the formula:



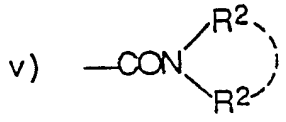
(I)

wherein A is
i) -NHCO-,
ii) -O-
iii) -$NHSO_2$-,
iv) -CO-
v) -CH_2- or

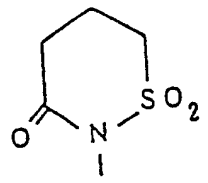
vi) -CH(OH)-;
W is i) C1-13 alkylene,
ii) phenylene or

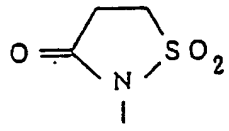
iii)  ;

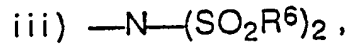
R^1 is i) hydrogen,
ii) C1-4 alkyl,
iii) -COOH,
iv) saturated or unsaturated, 4-7 membered mono-cyclic hetero ring containing one nitrogen as a hetero atom or saturated or unsaturated, 4-7 membered mono cyclic hetero ring containing one nitrogen as a hetero atom substituted by an oxo group,

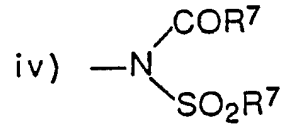
v) 

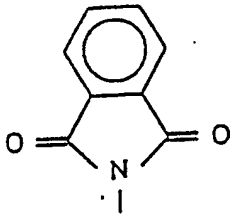
vi) $-CH_2OH$;
A, taken together with W and R^1, is

i)  ,

ii)  ,

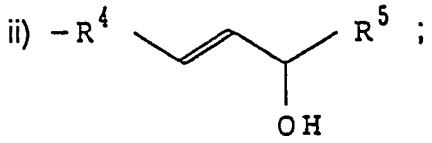
iii)  ,

iv)  or

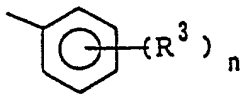
v)  ;

two R^2 are, same or different,
i) hydrogen,

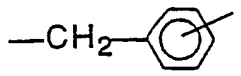
ii) C1-4 alkyl or
i) 4-7 membered, saturated or unsaturated, mono-cyclic hetero ring containing two or three of nitrogen and sulfur in total, or two R^2, taken together with a nitrogen to which they are attached, form saturated or unsaturated,
i) 7-14 membered, bi-or tri-cyclic hetero ring containing one nitrogen as a hetero atom, or
i) 4-7 membered, mono-cyclic hetero ring containing two or three of nitrogen and oxygen in total ;
Y is ethylene or vinylene;
D is i) -Z-B or

ii)  ;

Z is C3-11 alkylene or alkenylene

B is  ; or

Z, taken together with B, is C3-22 alkyl;
R^3 is i) hydrogen,
ii) halogen,
III) C1-8 alkyl, alkoxy or alkylthio, or
iv) C2-8 alkenyl, alkenyloxy or alkenylthio;
n is 1-3;
R^4 is C1-7 alkylene;
R^5 is i) C1-12 alkyl,
ii) C2-12 alkenyl,
iii) C5-7 cycloalkyl or
iv) phenethyl or phenethyl wherein the ring is substituted by one C1-4 alkoxy;
two R^6 are, same or different,
i) C1-7 alkyl,
ii) benzyl or
iii) phenyl or phenyl wherein the ring is substituted by one C1-4 alkyl; and
two R^7 are, same or different, C1-4 alky;
with the proviso that
i) -A-W-R^1 should bind to 3- or 4- carbon in benzene ring, and
ii) when W is phenylene or

 ,

A should not represent-O-, -CO-, $-CH_2-$ or -CH(OH)-;
and non-toxic salts thereof.
2) a compound according to claim 1, wherein A is -NHCO-.
3) A compound according to claim 2, which is
3-[1-[6-(4-methoxyphenyl)hex-5E-enyl]oxy-4-(5-oxo-5-morpholinopentanamido)benzen-2-yl]propionic acid,
3-[1-[6-(4-methoxyphenyl)hex-5E-enyl]oxy-4-(4-dimethylaminocarbonylbutanamido)benzen-2-yl]propionic acid,
3-[1-[6-(4-n-propoxyphenyl)hex-5E-enyl]oxy-4-(4-dimethylaminocarbonylbutanamido)benzen-2-yl]propionic acid,
3-[1-[6-[4-(2-propenyl)oxyphenyl]hex-5E-enyl]oxy-4-(4-dimethylaminocarbonylbutanamido)benzen-2-yl]-

propionic acid,
3-[1-[7-(4-methoxyphenyl)hept-6E-enyl]oxy-4-(4-dimethylaminocarbonylbutanamido)benzen-2-yl]propionic acid,
3-[1-[7-(4-methoxyphenyl)-n-heptyl]oxy-4-(4-dimethylaminocarbonylbutanamido)benzen-2-yl]propionic acid,
3-[1-[6-(4-methoxyphenyl)-n-hexyl]oxy-4-(4-dimethylaminocarbonylbutanamido)benzen-2-yl]propionic acid,
3-[1-[6-(4-methoxyphenyl)hex-5E-enyl]oxy-4-[4-(1-indolinyl)carbonylbutanamido]benzen-2-yl]propionic acid,
3-[1-[6-(4-methoxyphenyl)hex-5E-enyl]oxy-4-[4-(2-thiazolyl)aminocarbonylbutanamido]benzen-2-yl]propionic acid,
3-[1-[6-(4-methoxyphenyl)hex-5E-enyl]oxy-4-(3-dimethylaminocarbonylpropionamido)benzen-2-yl]propionic acid,
3-[1-[6-(4-methylthiophenyl)hex-5E-enyl]oxy-4-(4-dimethylaminocarbonylbutanamido)benzen-2-yl]propionic acid,
3-[1-[6-(4-methylphenyl)hex-5E-enyl]oxy-4-(4-dimethylaminocarbonylbutanamido)benzen-2-yl]propionic acid,
3-[1-[6-(4-chlorophenyl)hex-5E-enyl]oxy-4-(4-dimethylaminocarbonylbutanamido)benzen-2-yl]propionic acid,
3-[1-[6-(4-methoxyphenyl)hex-5E-enyl]oxy-4-(3-dimethylaminocarbonylbenzamido)benzen-2-yl]propionic acid,
3-[1-[6-(4-methoxyphenyl)hex-5E-enyl]oxy-4-(4-carboxylbutanamido)benzen-2-yl]proionic acid,
3-[1-[6-(4-methoxyphenyl)hex-5E-enyl]oxy-4-(4-carboxylbutanamido)benzen-2-yl]-E-acrylic acid,
3-[1-[6-(4-methoxyphenyl)hex-5E-enyl]oxy-4-(3-carboxylbenzamido)benzen-2-yl]propionic acid,
3-[1-[6-(4-methoxyphenyl)hex-5E-enyl]oxy-4-heptanamidobenzen-2-yl]propionic acid,
3-[1-[6-(4-methoxyphenyl)hex-5E-enyl]oxy-4-benzamidobenzen-2-yl]propionic acid,
3-[1-[6-(4-methoxyphenyl)hex-5E-enyl]oxy-4-acetamidobenzen-2-yl]propionic acid,
3-[1-[6-(4-methoxyphenyl)hex-5E-enyl]oxy-4-(5-hydroxypentanamido)benzen-2-yl]propionic acid,
3-[1-[6-(4-methoxyphenyl)hex-5E-enyl]oxy-4-(4-hydroxybutanamido)benzen-2-yl]propionic acid,
3-[1-[6-(4-methoxyphenyl)hex-5E-enyl]oxy-4-(3-hydroxymethylbenzamido)benzen-2-yl]propionic acid,
3-[1-(5E-7-hydroxypentadecenyl)oxy-4-(4-dimethylaminocarbonylbutanamido)benzen-2-yl]propionic acid, or
3-[1-[6-(4-methoxyphenyl)hex-5E-enyl]oxy-3-(4-dimethylaminocarbonylbutanamido)benzen-2-yl]propionic acid.

4) A compound according to claim 1, wherein A is -O-.

5) A compound according to claim 4, which is
3-[1-[6-(4-methoxyphenyl)hex-5E-enyl]oxy-4-(4-carboxylbutoxy)benzen-2-yl]propionic acid,
3-[1-(5E-7-hydroxy-n-pentadecenyl)oxy-4-(4-carboxylbutyl)oxybenzen-2-yl]propionic acid,
3-[1-[6-(4-methoxyphenyl)hex-5E-enyl]oxy-4-(4-dimethylaminocarbonylbutyl)oxybenzen-2-yl]propionic acid,
3-[1-(5E-7-hydroxy-n-pentadecenyl)oxy-4-(4-dimethylaminocarbonylbutyl)oxybenzen-2-yl]propionic acid,
3-[1-(5E-7-hydroxypentadecenyl)oxy-3-(4-dimethylaminocarbonylbutyl)oxybenzen-2-yl]propionic acid,
3-[1-(5E,9Z-7-hydroxy-n-pentadecenyl)oxy-4-(4-dimethylaminocarbonylbutyl)oxybenzen-2-yl]propionic acid,
3-[1-[5E-7-hydroxy-9-(4-methoxyphenyl)nonenyl]oxy-4-(4-carboxylbutyl)oxybenzen-2-yl]propionic acid,
3-[1-(5E-7-hydroxypentadecenyl)oxy-4-(3-carboxylpropyl)oxybenzen-2-yl]propionic acid,
3-[1-(5E-7-hydroxypentadecenyl)oxy-4-carboxylmethoxybenzen-2-yl]propionic acid,
3-[1-[6-(4-methoxyphenyl)hex-5E-enyl]oxy-4-n-propoxybenzen2-yl]propionic acid,
3-[1-[6-(4-methoxyphenyl)hex-5E-enyl]oxy-3-(4-dimethylaminocarbonylbutyl)oxybenzen-2-yl]propionic acid,
3-[1-(5E-6-methyl-7-hydroxy-n-pentadecenyl)oxy-4-(4-dimethylaminocarbonylbutyl)oxybenzen2-yl]propionic acid,
3-[1-[6-(4-methoxyphenyl)hex-5E-enyl]oxy-4-(3-dimethylaminocarbonyl-n-propyl)oxybenzen-2-yl]propionic acid,
3-[1-[6-(4-methoxyphenyl)hex-5E-enyl]oxy-3-(3-carboxylpropyl)oxybenzen-2-yl]propionic acid,
3-[1-[6-(4-methoxyphenyl)hex-5E-enyl]oxy-3-(4-carboxylbutyl)oxybenzen-2-yl]propionic acid,
3-[1-[6-(4-methoxyphenyl)hex-5E-enyl]oxy-3-(4-(2-pyrrolidon-1-yl)-n-butoxy]benzen-2-yl]propionic acid,
3-[1-[6-(4-methoxyphenyl)hexyl]oxy-3-(4-dimethylaminocarbonylbutyl)oxybenzen-2-yl]propionic acid or
3-[1-[6-(4-methoxyphenyl)hexyl]oxy-3-(4-carboxylbutyl)oxybenzen-2-yl]propionic acid.

6) A compound according to claim 1, wherein A is -$NHSO_2$-

7) A compound according to claim 6, which is
3-[1-[6-(4-methoxyphenyl)hexyl]oxy-4-(4-methylphenyl)sulfonylaminobenzen-2-yl]propionic acid,
3-[1-[6-(4-methoxyphenyl)hexyl]oxy-4-(3-dimethylaminocarbonyl-n-propyl)sulfonylaminobenzen-2-yl]-propionic acid,
3-[1-[6-(4-methoxyphenyl)hex-5E-enyl]oxy-4(4-methylphenyl)sulfonylaminobenzen-2-yl]propionic acid,
3-[1-[6-(4-methoxyphenyl)hex-5E-enyl]oxy-4-(3-dimethylaminocarbonyl-n-propyl)sulfonylaminobenzen-2-yl]-propionic acid,

3-[1-[6-(4-methoxyphenyl)hex-5E-enyl]oxy-4-methylsulfonylaminobenzen-2-yl]propionic acid,
3-[1-[6-(4-methoxyphenyl)hex-5E-enyl]oxy-4-benzylsulfonylaminobenzen-2-yl]propionic acid,
or
3-[1-[6-(4-methoxyphenyl)hex-5E-enyl]oxy-4-(3-carbonylpropyl)sulfonylaminobenzen-2-yl]propionic acid.

8) A compound according to claim 1, wherein A is -CO-.

9) A compound according to claim 8, which is
3-[1-6-(4-methoxyphenyl)hex-5E-enyl]oxy-4-(1-oxo-4-dimethylaminocarbonylbutyl)benzen-2-yl]propionic acid,
3-[1-6-(4-methoxyphenyl)hex-5E-enyl]oxy-3-(1-oxo-5-carboxylpentyl)benzen-2-yl]propionic acid,
3-[1-6-(4-methoxyphenyl)hex-5E-enyl]oxy-3-(1-oxo-5-dimethylaminocarbonylpentyl)benzen-2-yl]propionic acid,
3-[1-6-(4-methoxyphenyl)hex-5E-enyl]oxy-4-(1-oxo-4-carboxylbutyl)benzen-2-yl]propionic acid,
3-[1-6-(4-methoxyphenyl)hex-5E-enyl]oxy-4-(1-oxo-5-carboxylpentyl)benzen-2-yl]propionic acid or
3-[1-6-(4-methoxyphenyl)hex-5E-enyl]oxy-4-(1-oxo-5-dimethylaminocarbonylpentyl]benzen-2-yl]propionic acid.

10) A compound according to claim 1, wherein A is $-CH_2-$.

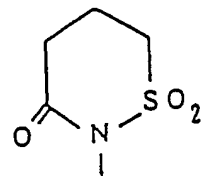
11) A compound according to claim 10, which is
3-[1-[6-(4-methoxyphenyl)hex-5E-enyl]oxy-4-(4-carboxylbutyl)benzen-2-yl]propionic acid,
3-[1-[6-(4-methoxyphenyl)hex-5E-enyl]oxy-4-(4-dimethylaminocarbonylbutyl)benzen-2-yl]propionic acid,
3-[1-(5E-7-hydroxy-n-pentadecenyl)oxy-4-(4-dimethylaminocarbonyl-n-butyl)benzen-2-yl]propionic acid,
3-[1-(5E-7-hydroxy-n-pentadecenyl)oxy-4-(4-carboxylbutyl)benzen-2-yl]propionic acid,
3-[1-[6-(4-methoxyphenyl)hex-5E-enyl]oxy-4-n-butylbenzen-2-yl]propionic acid,
3-[1-[6-(4-methoxyphenyl)hex-5E-enyl]oxy-3-(5-carboxylpentyl)benzen-2-yl]propionic acid,
3-[1-[6-(4-methoxyphenyl)hex-5E-enyl]oxy-3-(5-dimethylaminocarbonylpentyl)benzen-2-yl]propionic acid,
3-[1-[6-(4-methoxyphenyl)hex-5E-enyl]oxy-4-(5-carboxylpentyl)benzen-2-yl]propionic acid or
3-[1-[6-(4-methoxyphenyl)hex-5E-enyl]oxy-4-(5-dimethylaminocarbonylpentyl)benzen-2-yl]propionic acid.

12) A compound according to claim 1, wherein A is -CH(OH)-.

13) A compound according to claim 12, which is
3-[1-[6-(4-methoxyphenyl)hex-5E-enyl]oxy-4-(1-hydroxy-4-dimethylaminocarbonylbutyl)benzen-2-yl]-propionic acid
3-[1-[6-(4-methoxyphenyl)hex-5E-enyl]oxy-3-(1-hydroxy-5-carboxylpentyl)benzen-2-yl]propionic acid
3-[1-[6-(4-methoxyphenyl)hex-5E-enyl]oxy-3-(1-hydroxy-5-dimethylaminocarbonylpentyl)benzen-2-yl]-propionic acid
3-[1-[6-(4-methoxyphenyl)hex-5E-enyl]oxy-4-(1-hydroxy-4-carboxylbutyl)benzen-2-yl]propionic acid
3-[1-[6-(4-methoxyphenyl)hex-5E-enyl]oxy-4-(1-hydroxy-5-carboxylpentyl)benzen-2-yl]propionic acid
or
3-[1-[6-(4-methoxyphenyl)hex-5E-enyl]oxy-4-(1-hydroxy-5-dimethylaminocarbonylpentyl)benzen-2-yl]-propionic acid.

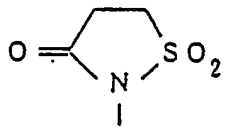
14) A compound according to claim 1, wherein
A, taken together with W and R1, is

i)



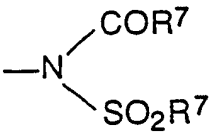
,

ii)



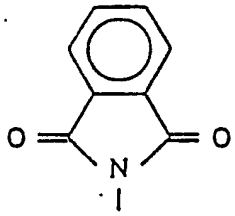
,

iii) $-N-(SO_2R^6)_2$,

iv) 

or

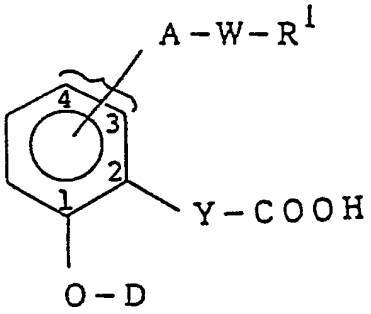
v)



.

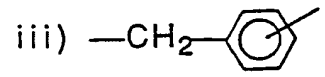
15) A compound according to claim 14, which is
3-[1-[6-(4-methoxyphenyl)hexyl]oxy-4-(perhydro-1,2-thiazin-1,1,3-trione-2-yl)benzen-2-yl]propionic acid,
3-[1-[6-(4-methoxyphenyl)hex-5E-enyl]oxy-4-(perhydro-1,2-thiazin-1,1,3-trione-2-yl]benzen-2-yl]propionic acid,
3-[1-[6-(4-methoxyphenyl)hex-5E-enyl]oxy-4-(isothiazolidin-1,1,3-trione-2-yl)benzen-2-yl]propionic acid,
3-[1-[6-(4-methoxyphenyl)hex-5E-enyl]oxy-4-phthalimidobenzen-2-yl]propionic acid,
3-[1-[6-(4-methoxyphenyl)hex-5E-enyl]oxy-4-(N-acetyl-N-mesyl)aminobenzen-2-yl]propionic acid,
3-[1-[6-(4-methoxyphenyl)hex-5E-enyl]oxy-4-dimesylaminobenzen-2-yl]propionic acid,
3-[1-(5E-7-hydroxy-n-pentadecenyl)oxy-4-(perhydro-1,2-thiazin-1,1,3-trione-2-yl)benzen-2-yl]propionic acid,
3-[1-[6-(4-methoxyphenyl)hex-5E-enyl]oxy-4-bis(n-butylsulfonyl)aminobenzen-2-yl]propionic acid,
3-[1-(5E-7-hydroxy-n-pentadecenyl)oxy-4-dimesylaminobenzen-2-yl]propionic acid,
3-[1-[6-(4-methoxyphenyl)hex-5E-enyl]oxy-3-dimesylaminobenzen-2-yl]propionic acid
or
3-[1-[6-(4-methoxyphenyl)hex-5E-enyl]oxy-3-(perhydro-1,2-thiazin-1,1,3-trione-2-yl)benzen-2-yl]propionic acid.

16) A process for the preparation of compounds of the formula:

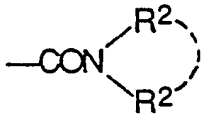


(I)

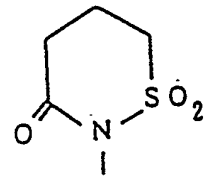
wherein A is
i) -NHCO-,
ii) -O-
iii) -$NHSO_2$-,
iv) -CO-
v) -CH_2- or
vi) -CH(OH)-;
W is i) C1-13 alkylene,
ii) phenylene or

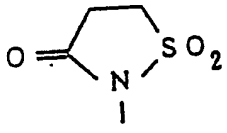
iii)  ;

R^1 is i) hydrogen,
ii) C1-4 alkyl,
iii) -COOH,
iv) saturated or unsaturated, 4-7 membered mono-cyclic hetero ring containing one nitrogen as a hetero atom or saturated or unsaturated, 4-7 membered monocyclic hetero ring containing one nitrogen as a hetero atom substituted by an oxo group,

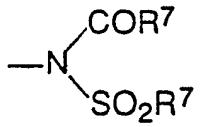
v) 

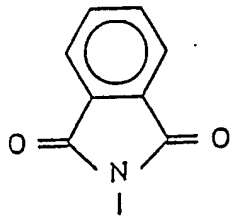
vi) -CH_2OH;
A, taken together with W and R^1, is

i)  ,

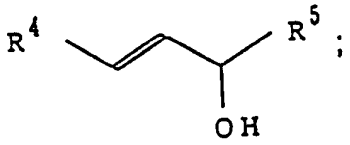
ii)  ,

iii) -N-$(SO_2R^6)_2$,

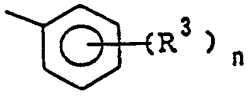
iv)  or

v)  ;

two R^2 are, same or different,
i) hydrogen,
ii) C1-4 alkyl or
iii) 4-7 membered, saturated or unsaturated, mono-cyclic hetero ring containing two or three of nitrogen and sulfur in total, or two R^2, taken together with a nitrogen to which they are attached, form saturated or unsaturated,
i) 7-14 membered, bi-or tri-cyclic hetero ring containing one nitrogen as a hetero atom, or
ii) 4-7 membered, mono-cyclic hetero ring containing two or three of nitrogen and oxygen in total ;
Y is ethylene or vinylene;
D is i) -Z-B or

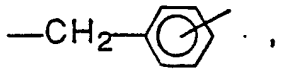
ii)  ;

Z is C3-11 alkylene or alkenylene
B is

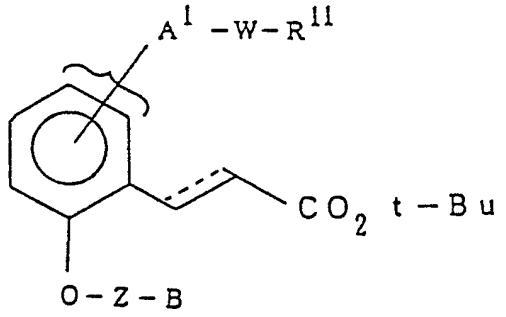


; or
Z, taken together with B, is C3-22 alkyl;
R^3 is i) hydrogen,
ii) halogen,
iii) C1-8 alkyl, alkoxy or alkylthio, or
iv) C2-8 alkenyl, alkenyloxy or alkenylthio;
n is 1-3;
R^4 is C1-7 alkylene;
R^5 is i) C1-12 alkyl,
ii) C2-12 alkenyl,
iii) C5-7 cycloalkyl or
iv) phenethyl or phenethyl wherein the ring is substituted by one C1-4 alkoxy;
Two R^6 are, same or different,
i) C1-7 alkyl,
ii) benzyl or

iii) phenyl or phenyl wherein the ring is substituted by one C1-4 alkyl; and
Two R^7 are, same or different, C1-4 alky;
with the proviso that
i) -A-W-R^1 should bind to 3- or 4- carbon in benzene ring, and
ii) when W is phenylene or

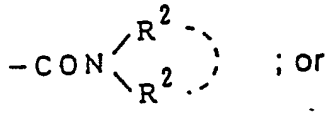


A should not represent -O-, -CO-, -CH_2- or -CH(OH)-;
and non-toxic salts thereof,
which is characterized by:
(1) saponificating the compound of the formula:



(II)

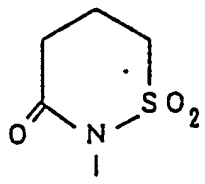
wherein A^1 is
i) -NHCO- or
ii) -$NHSO_2$-;
R^{11} is
i) the group of R^{1a}
(wherein R^{1a} is hydrogen, saturated or unsaturated, 4-7 membered mono-cyclic hetero ring containing one nitrogen as a hetero atom, unsubstituted or substituted by an oxo group or C1-C4 alkyl),
ii) -CO_2H or
iii) the group shown by:

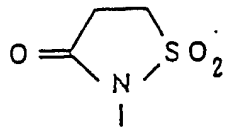


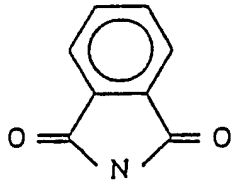
; or

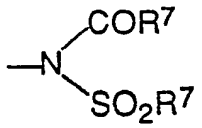
A^1, taken together with W and R^{11}, is

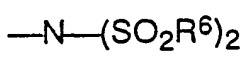
i)



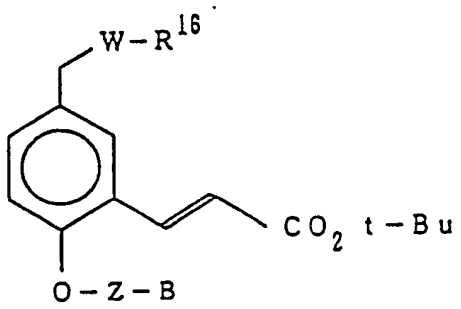
ii) 

iii) 

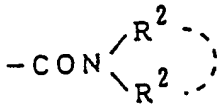
iv)  or

v)  ;

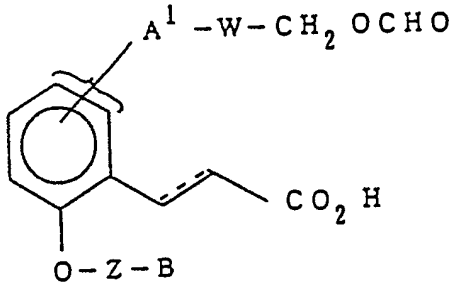
is ethylene or vinylene;
t-Bu is tert-Butyl group; and
the other symbols are the same meanings as described hereinbefore;
or the compounds of the formula:

 (XI)

wherein R^{16} is
i) $-CO_2H-$ or
ii) the group of the formula:

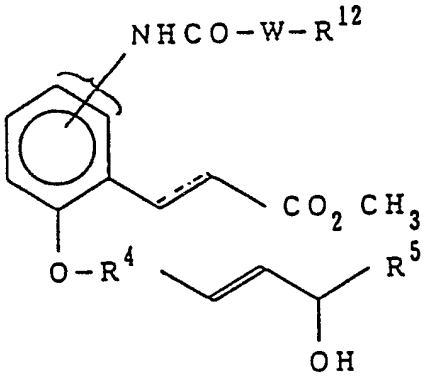
 ; and

the other symbols are the same meanings as described hereinbefore;
with using an acid (formic acid, trifluoroacetic acid etc.) ,
(2) saponificating the compound of the formula:



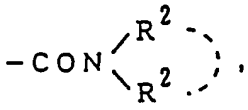
(III)

wherein, all of the symbols are same meaning as described hereinbefore;,
the compound of the formula:



(IV)

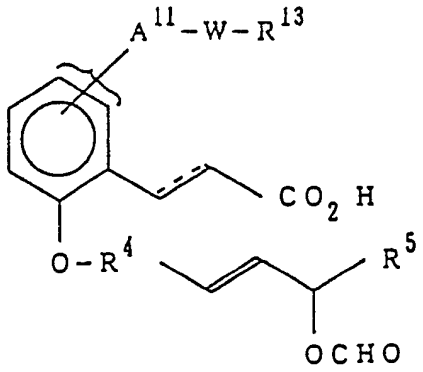
wherein R^{12} is
i) the group of R^{1a},
ii) the group shown by



iii) $-CO_2CH_3$ or

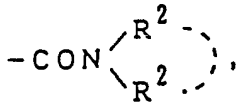
IV)  ; and

the other symbols are the same meanings as described hereinbefore;,
the compound of the formula:



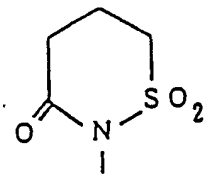
(V)

wherein A^{11} is $-NHSO_2-$;
R^{13} is
i) the group of $-R^{1a}$,
ii) the group shown by

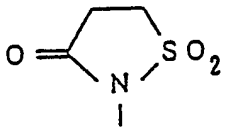


iii) $-CH_2OCHO$ or
iv) $-CO_2H$;
A^{11}, taken together with W and R^{13}, is

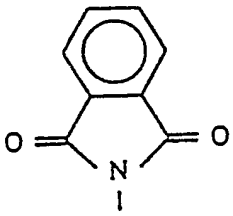
i)

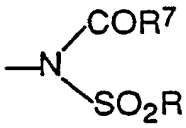


ii)



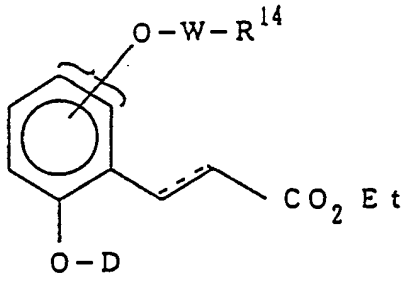
iii)



iv)  or

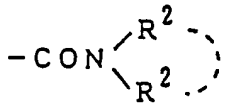
v) $—N(SO_2R^6)_2$; and

the other symbols are the same meanings as described hereinbefore;,
the compound of the formula:



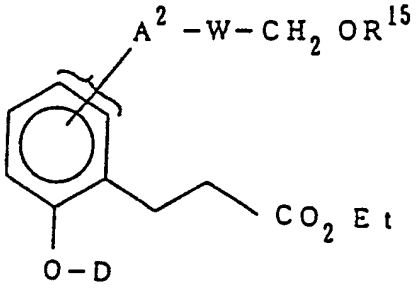
(VI)

wherein Et is ethyl;
R^{14} is
i) the group of $-R^{1a}$,
ii) the group shown by

 or

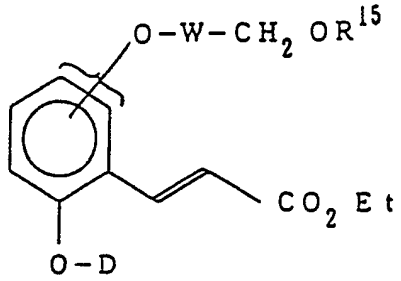
iii) $-CO_2Et$; and

the other symbols are the same meanings as described hereinbefore;,
the compound of the formula:



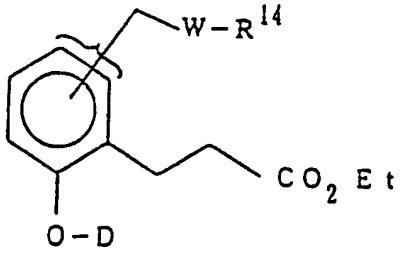
(VII)

wherein A^2 is
i) -O- or
ii) $-CH_2-$;
R^{15} is
i) hydrogen or
ii) acetyl group; and
the other symbols are the same meanings as described hereinbefore;,
the compound of the formula:



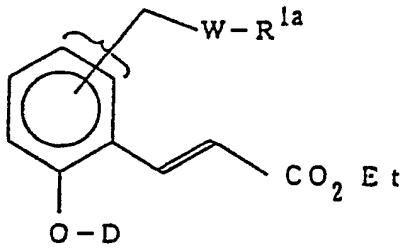
(VIII)

wherein all of the symbols are the same meanings as described hereinbefore;,
the compound of the formula:



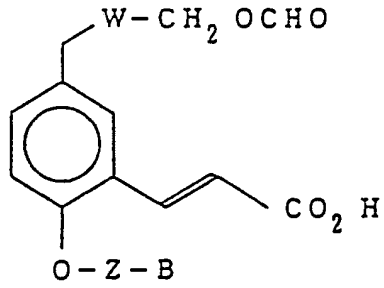
(IX)

wherein all of the symbols are the same meanings as described hereinbefore;,
the compound of the formula:



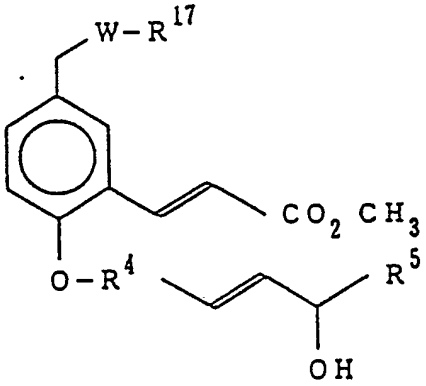
(X)

wherein all of the symbols are the same meanings as described hereinbefore;, the compound of the formula;



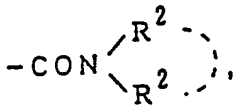
(XII)

wherein all of the symbols are the same meanings as described hereinbefore;, the compound of the formula:

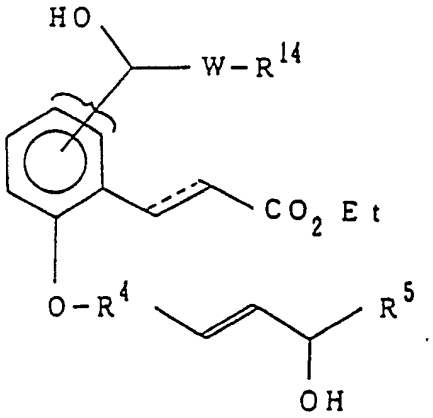


(XIII)

wherein R^{17} is
i) the group shown by

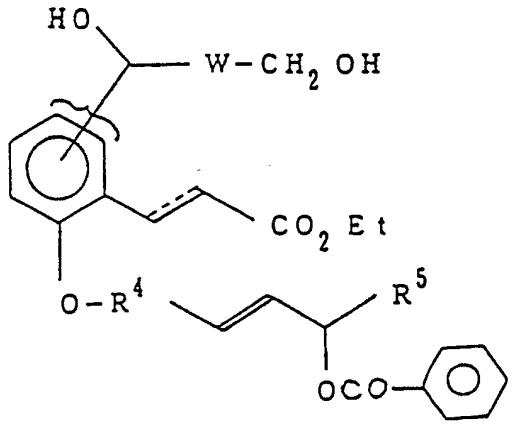


ii) $-CH_2OH$ or
iii) $-CO_2H$; and
the other symbols are the same meanings as described hereinbefore;, the compound of the formula:



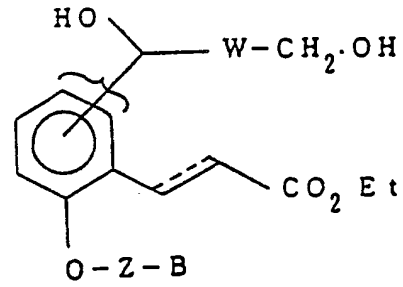
(XV)

wherein all of the symbols are the same meanings as described hereinbefore;, the compound of the formula:



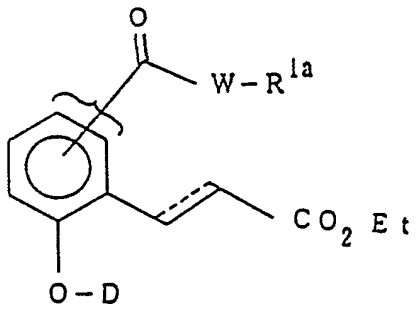
(XVI)

wherein all of the symbols are the same meanings as described hereinbefore;, the compound of the formula:



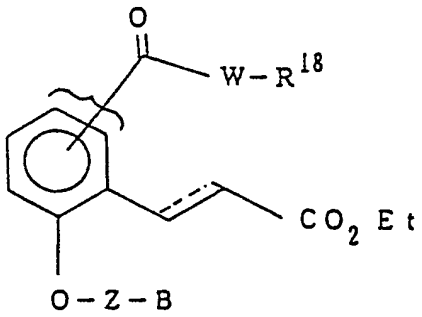
(XVII)

wherein all of the symbols are the same meanings as described hereinbefore;, the compound of the formula:



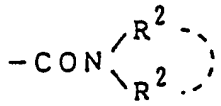
(XVIII)

wherein all of the symbols are the same meanings as described hereinbefore;,
the compound of the formula:

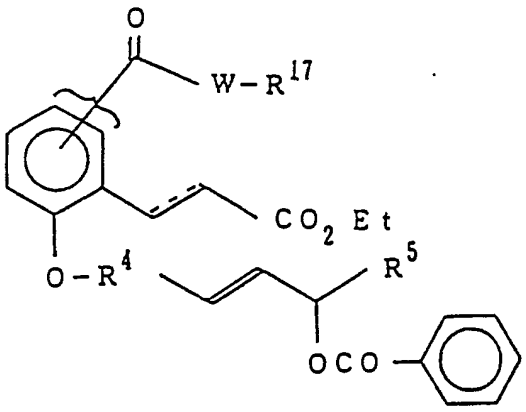


(XIX)

wherein R^{18} is
i) $-CO_2Et$,
ii) the group shown by

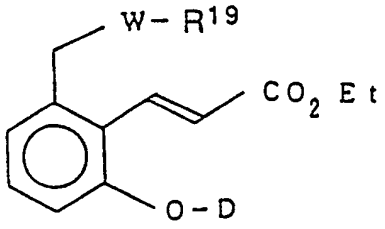


or
iii) $-CH_2OH$; and
the other symbols are the same meanings as described hereinbefore;,
the compound of the formula:



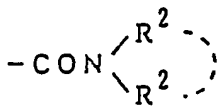
(XX)

wherein, all of the symbols are the same meanings as described hereinbefore;,
the compound of the formula:



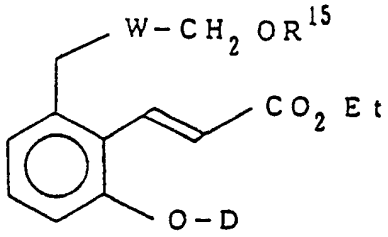
(XXI)

wherein R^{19} is
i) the group shown by



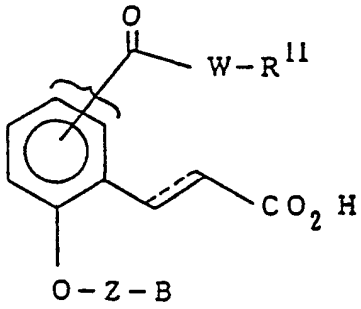
or

ii) $-CO_2Et$; and
the other symbols are the same meanings as described hereinbefore; or
the compound of the formula:



(XXII)

wherein all of the symbols are the same meanings as described hereinbefore;
with using an alkali (sodium hydroxide etc.) ,
(3) reducing the compound of the formula:



(XIV)

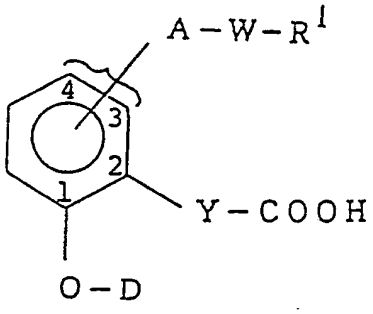
wherein all of the symbols are the same meanings as described hereinbefore ; or
(4) converting the compound of the formula (I) into the corresponding salt thereof, if necessary.

17) A pharmaceutical composition which comprise, as active ingredient, the phenylalkan(en)oic acid of the formula (I) as claimed in claim 1, or the pharmaceutically acceptable acid addition salts thereof.

18) For use in the prevention and/or treatment of several diseases induced by leukotriene B4, the phenylalkan(en)oic acid of the formula (I) as claimed in claim 1, or the pharmaceutically acceptable acid addition salts thereof.

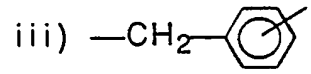
Claims for the following Contracting States: ES, GR

1) A process for the preparation of compounds of the formula:

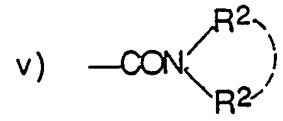


(I)

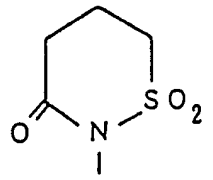
wherein A is
i) -NHCO-,
ii)-O-
iii) -$NHSO_2$-,
iv) -CO-
v) -CH_2- or
vi) -CH(OH)-;
W is i) C1-13 alkylene,
ii) phenylene or

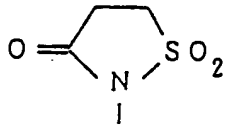
iii)  ;

R^1 is i) hydrogen,
ii) C1-4 alkyl,
iii) -COOH,
iv) saturated or unsaturated, 4-7 membered mono-cyclic hetero ring containing one nitrogen as a hetero atom or saturated or unsaturated, 4-7 membered monocyclic hetero ring containing one nitrogen as a hetero atom substituted by an oxo group,

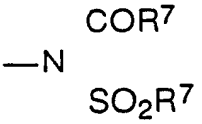
v) 

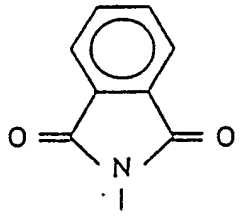
vi) -CH_2OH;
A, taken together with W and R^1, is

i)  ,

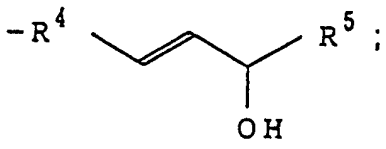
ii)  ,

iii) $-N-(SO_2R^6)_2$,

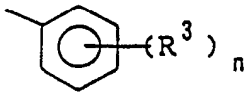
iv)  or

v)  ;

two R^2 are, same or different,
i) hydrogen,
ii) C1-4 alkyl or
iii) 4-7 membered, saturated or unsaturated, mono-cyclic hetero ring containing two or three of nitrogen and sulfur in total, or two R^2, taken together with a nitrogen to which they are attached, form saturated or unsaturated,
i) 7-14 membered, bi-or tri-cyclic hetero ring containing one nitrogen as a hetero atom, or
ii) 4-7 membered, mono-cyclic hetero ring containing two or three of nitrogen and oxygen in total ;
Y is ethylene or vinylene;
D is i) -Z-B or

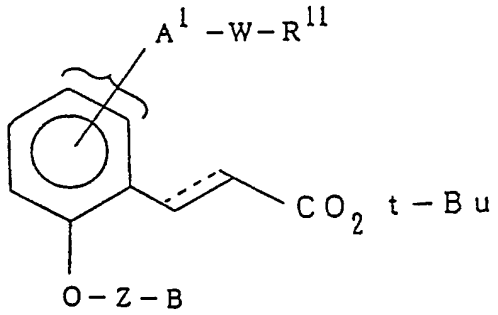
ii)  ;

Z is C3-11 alkylene or alkenylene
B is

 ; or

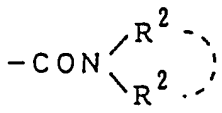
Z, taken together with B, is C3-22 alkyl;
R^3 is i) hydrogen,
ii) halogen,
iii) C1-8 alkyl, alkoxy or alkylthio, or
iv) C2-8 alkenyl, alkenyloxy or alkenylthio;
n is 1-3;
R^4 is C1-7 alkylene;
R^5 is i) C1-12 alkyl,
ii) C2-12 alkenyl,
iii) C5-7 cycloalkyl or
iv) phenethyl or phenethyl wherein the ring is substituted by one C1-4 alkoxy;
Two R^6 are, same or different,
i) C1-7 alkyl,
ii) benzyl or
iii) phenyl or phenyl wherein the ring is substituted by one C1-4 alkyl; and
Two R^7 are, same or different, C1-4 alky;
with the proviso that
i) -A-W-R^1 should bind to 3- or 4- carbon in benzene ring, and
ii) when W is phenylene or -CH_2-, A should not represent -O-, -CO-, -CH_2- or-CH(OH)-;
and non-toxic salts thereof,
which is characterized by:

(1) saponificating the compound of the formula:



(II)

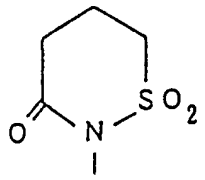
wherein A^1 is
i) -NHCO- or
ii) -$NHSO_2$-;
R^{11} is
i) the group of R^{1a}
(wherein R^{1a} is hydrogen, saturated or unsaturated, 4-7 membered mono-cyclic hetero ring containing one nitrogen as a hetero atom, unsubstituted or substituted by an oxo group or C1-C4 alkyl),
ii) -CO_2H or
iii) the group shown by:



; or

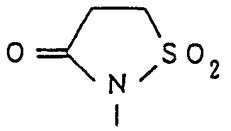
A^1, taken together with W and R^{11}, is

i)



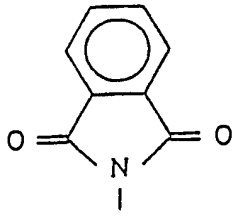
,

ii)

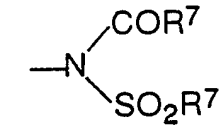


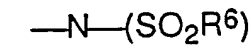
,

iii)



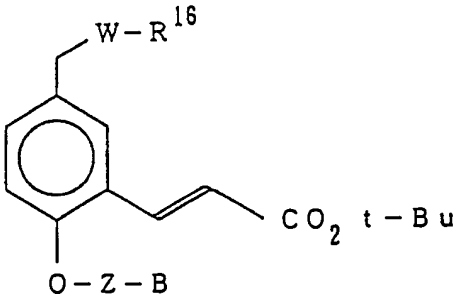
,

iv)  or

v)  ;

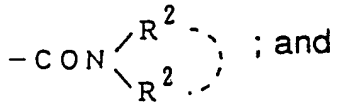
 is ethylene or vinylene;

t-Bu is tert-Butyl group; and
the other symbols are the same meanings as described hereinbefore;
or the compounds of the formula:



(XI)

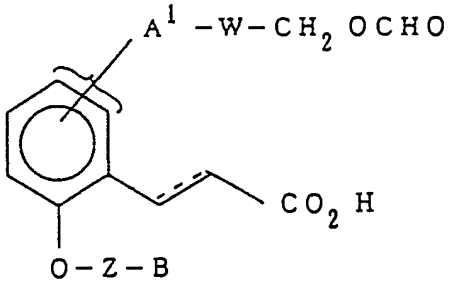
wherein R^{16} is
i) $-CO_2H$ or
ii) the group of the formula:



; and

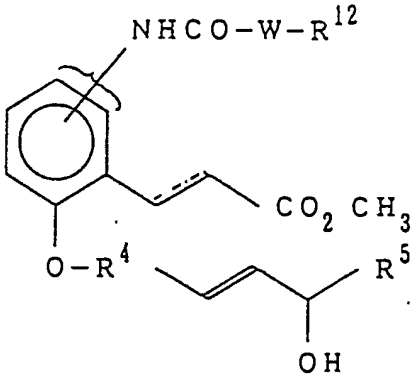
the other symbols are the same meanings as described hereinbefore;

with using an acid (formic acid, trifluoroacetic acid etc.),
(2) saponificating the compound of the formula:



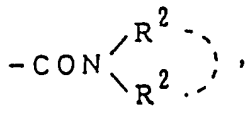
(III)

wherein, all of the symbols are same meaning as described hereinbefore;
the compound of the formula:

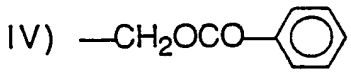


(IV)

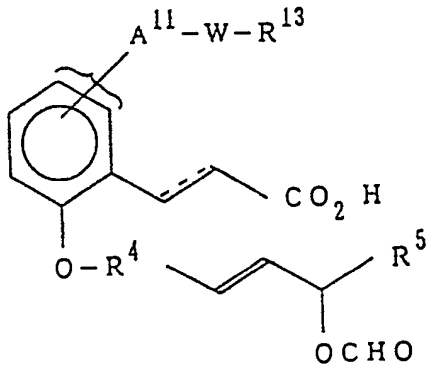
wherein R^{12} is
i) the group of R^{1a},
ii) the group shown by



iii) $-CO_2CH_3$ or

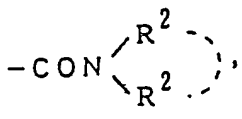
IV)  ; and

the other symbols are the same meanings as described hereinbefore;,
the compound of the formula:



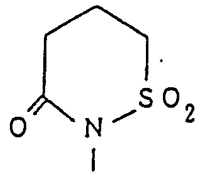
(V)

wherein A^{11} is $-NHSO_2-$;
R^{13} is
i) the group of $-R^{1a}$,
ii) the group shown by



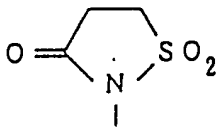
iii) $-CH_2OCHO$ or
iv) $-CO_2H$;
A^{11}, taken together with W and R^{13}, is

i)



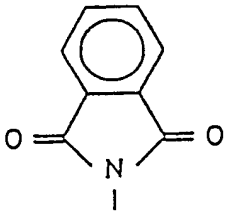
,

ii)

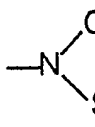


,

iii)

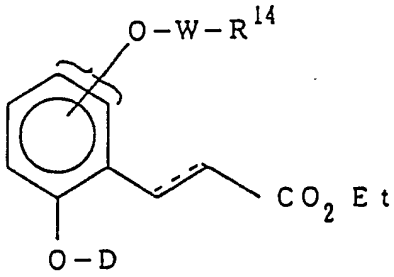


,

iv)  or

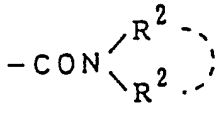
v) $-N(SO_2R^6)_2$; and

the other symbols are the same meanings as described hereinbefore;,
the compound of the formula:



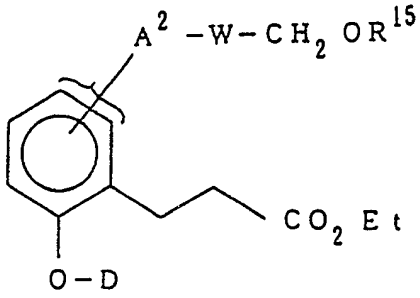
(VI)

wherein Et is ethyl;
R^{14} is
i) the group of $-R^{1a}$,
ii) the group shown by

 or

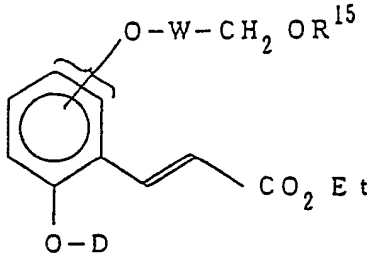
iii) $-CO_2Et$; and
the other symbols are the same meanings as described hereinbefore;,

the compound of the formula:



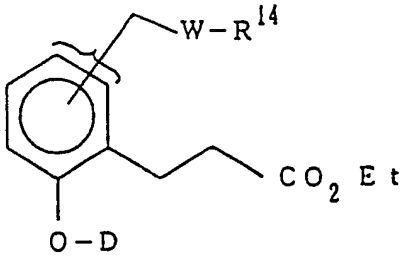
(VII)

wherein A^2 is
i) -O- or
ii) $-CH_2-$;
R^{15} is
i) hydrogen or
ii) acetyl group; and
the other symbols are the same meanings as described hereinbefore;,
the compound of the formula:



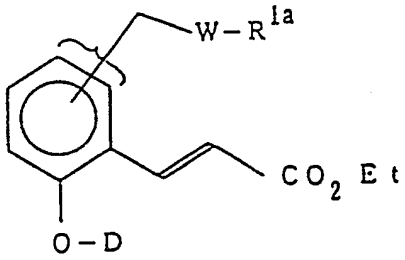
(VIII)

wherein all of the symbols are the same meanings as described hereinbefore;,
the compound of the formula:



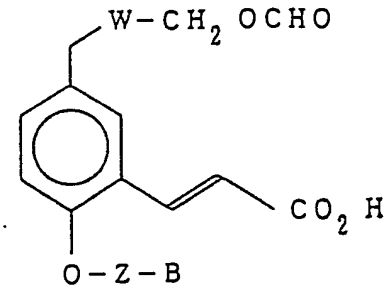
(IX)

wherein all of the symbols are the same meanings as described hereinbefore;,
the compound of the formula:



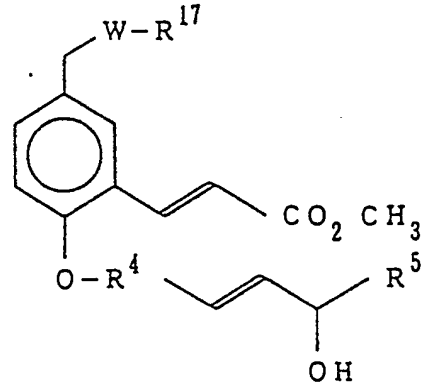
(X)

wherein all of the symbols are the same meanings as described hereinbefore;, the compound of the formula;



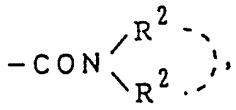
(XII)

wherein all of the symbols are the same meanings as described hereinbefore;, the compound of the formula:

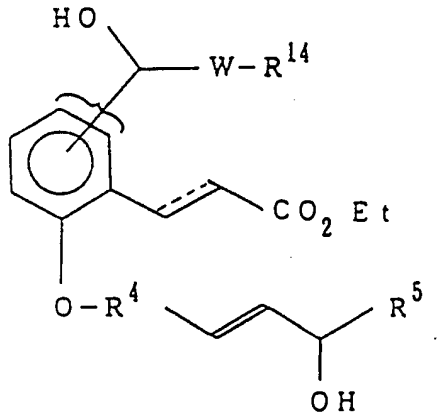


(XIII)

wherein R^{17} is
i) the group shown by

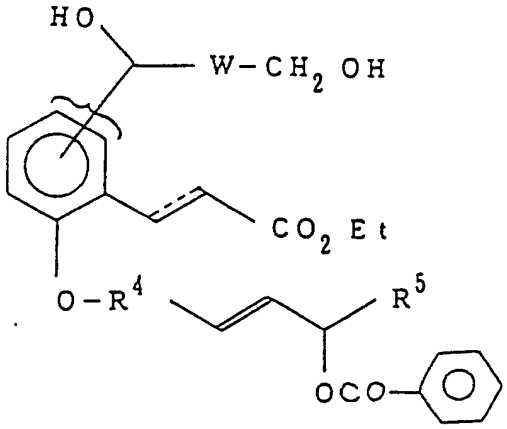


ii) $-CH_2OH$ or
iii) $-CO_2H$; and
the other symbols are the same meanings as described hereinbefore;, the compound of the formula:



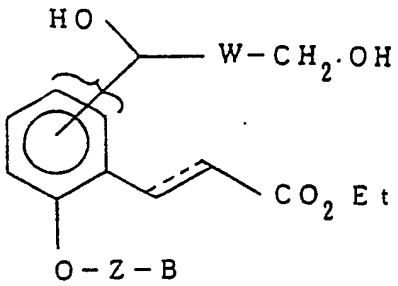
(XV)

wherein all of the symbols are the same meanings as described hereinbefore;, the compound of the formula:



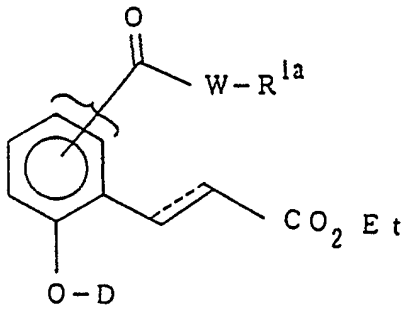
(XVI)

wherein all of the symbols are the same meanings as described hereinbefore;, the compound of the formula:



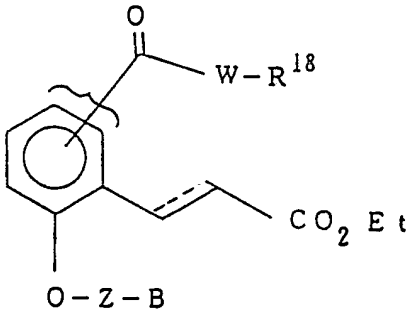
(XVII)

wherein all of the symbols are the same meanings as described hereinbefore;, the compound of the formula:



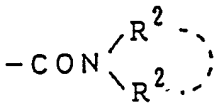
(XVIII)

wherein all of the symbols are the same meanings as described hereinbefore;,
the compound of the formula:

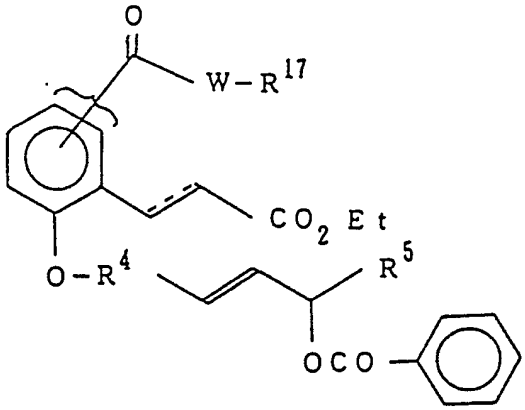


(XIX)

wherein R^{18} is
i) $-CO_2Et$,
ii) the group shown by



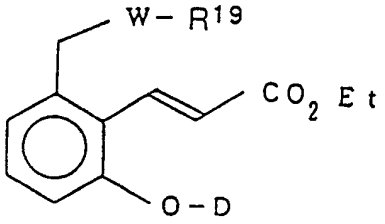
or
iii) $-CH_2OH$; and
the other symbols are the same meanings as described hereinbefore;,
the compound of the formula:



(XX)

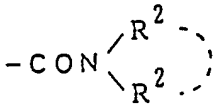
wherein, all of the symbols are the same meanings as described hereinbefore;,

the compound of the formula:



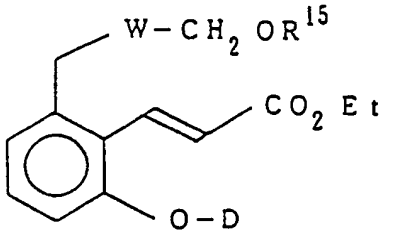
(XXI)

wherein R^{19} is
i) the group shown by



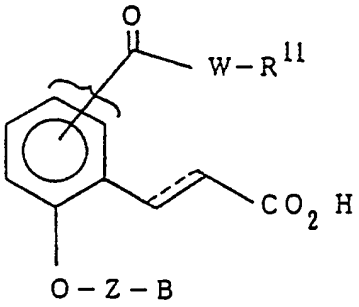
or

ii) $-CO_2Et$; and
the other symbols are the same meanings as described hereinbefore; or
the compound of the formula:



(XXII)

wherein all of the symbols are the same meanings as described hereinbefore;
with using an alkali (sodium hydroxide etc.) ,
(3) reducing the compound of the formula:



(XIV)

wherein all of the symbols are the same meanings as described hereinbefore ; or
(4) converting the compound of the formula (I) into the corresponding salt thereof, if necessary.